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EDITORIAL

SPECIALIZATION

WHERE DO WE GO FROM HERE

IN general terms it may be said that Americans have been cordial to the theory and practice of specialization not only in medicine but in all fields. It is a current overstatement, but containing a germ of truth, that "America is a nation of specialists." Now a good case can be made for two quite opposed propositions: (1) we have gone so far in encouraging specialization that we have an insufficient supply of people whose knowledge makes them capable judges of broad fields; (2) the increase in the actual amount of human knowledge is so great that in many or most fields it is quite beyond the grasp of a single mind. But in fact both these propositions are in part true and in part false. It is true that the whole is less well seen than it was two or three generations ago but the whole is larger. If we accept the proposition that a grasp of a large field of human knowledge requires very accurate and up to date information on all of the facts therein concerned, we must accept the conclusion. On the other hand, one may easily come to the conclusion that too large a mass of facts may interfere with sound generalizations. Perhaps the answer is that, though it may take an unusual type of mind to select those facts which are essential and discard those which are unessential, such minds exist and, what is perhaps more important, can be developed by proper training. In this way one might easily accept the premise but deny the conclusion, which apparently is that we should abandon or limit specialization in order to supply ourselves with a group of people capable of grasping the general implications and directing progress.

In regard to the second proposition, it will be difficult to deny the evidence that much of the rapid progress of the last quarter of a century has been the direct result of our cordiality to specialization. Not a little of the outstanding contributions to human knowledge made by specialists has

been the direct result of our willingness to grant them opportunity and not press them too fiercely for material results. It cannot, however, be denied that men capable of sound broad generalization will be essential to orderly progress.

Our theoretical cordiality to specialization has now existed long enough to entitle us to draw certain conclusions, at least in the field of medical science and medical practice. Confining ourselves now to this field, it is interesting to note that the British theory of medical education and medical organization of hospitals and laboratories has followed a distinctly different line. They have been inclined to stress the development of the general man either in medicine or surgery and have geared to this objective not only their teaching of undergraduates but their hospital organization and their teaching of graduate students. Their clinical teaching is largely conducted by internists and general surgeons, and they have been reluctant to establish in their great teaching hospitals separate departments for the development of the special fields. They have perhaps taken the view that the man with the broad general training who has an uncontrollable yearning for work in some special field will be able to find for himself sufficient opportunity and a satisfactory niche much as have the men working in the fundamental sciences. As the result of this policy, it has seemed to me that viewed as a whole their general practitioners were better trained and wiser people than ours. Of this I do not feel sure but I do feel quite sure that as the result of their policy they have failed to develop as large a proportion of outstanding men in the special fields as has been the case in this country where we have followed the opposite policy.

Coming now to the consideration of our own situation, which is our only proper concern, it is worthwhile to note that as a result of our cordiality to the training and development of specialists, we find ourselves in the interesting situation in which the general practitioner is the least experienced and least trained man in our medical hierarchy. Now unless we abandon our traditional view of the relation of the general practitioner to the field of medicine, we have here the man in the largest and most difficult field least well equipped for his admittedly gigantic task. I have elsewhere[1] had occasion to state my view that we may wisely accept the proposition that all medicine is today in fact specialized. Since in this quasi-philosophical discussion it is essential that one define one's terms, I will define a specialist as one who has had a training differing from that of this brethren in other fields and planned for the purpose of equipping him for the work that he plans to do. There has been general acceptance of the view that one who aspires to be ranked as a specialist in one of the subdivisions of the practice of medicine will require not only a basic training but more or less prolonged special training in the field of his concentration. I suggest that if this is a sound proposition in regard to the adequate preparation of men for the more circumscribed fields, it is even more true of those who aspire to the difficult task of seeing the bulk of the population in the first instance, recognizing with reasonable accuracy the nature of their disabilities and advising them in regard to the methods of relief.

The medical profession at the present time in this country may be described as a hierarchy at the head of which is, or should be, the general practitioner who in turn is flanked by the internist and the general surgeon. Next come an almost bewildering group of specialists. These subdivisions have taken place by age groups as in pediatrics—why not also specialists in the care of the aged—by sex as in obstetrics and gynecology, by systems of organs as in genito-urinary medicine, gastroenterology, diseases of the nervous system, diseases of the circulation—finally, though not exclusively, by organs such as the eye, ear, nose, throat, heart, lung, and kidney. Moreover, our tendency to subdivide the field is obviously not yet at an end, and

though we may continue to support the view that progress is likely to be best achieved by such subdivision, we cannot, of course, blind ourselves to the dangers inherent in such a plan.

DANGERS OF SPECIALISTS

From the outset there has been complete, perhaps too complete, recognition of the danger that contraction of the field of work may also contract the field of vision. There has been a constant rear guard action between the more or less retreating general practitioner and the advancing horde of specialists. It is not clear to me that these rear guard actions have on the whole been productive of good results and often they have shed upon the subject more heat than light. It is quite conceivable that our plans for the future might properly call a halt to reiteration and abuse and take the form of a broader plan by which we can strengthen the various parts of our hierarchy above referred to and provide for better articulation between the various fields.

But there is another danger of specialization to which I have seen less reference and which seems to me important. I refer to the effect of specialization, particularly in the narrower fields, upon the character of the specialist. It has seemed to me that for the younger man mastery of a subdivision of the field of medicine is an almost necessary prerequisite to the attainment of real mastery in a larger field. This, however, is quite a different proposition from the assertion that mastery of a special field can be continued throughout life without reacting unfavorably upon the individual. I think one can see the evidence that such a reaction takes place, that the mastery by the expert of a special field is at its best at that period which we lightheartedly refer to as middle life, but may later turn and crush him like a Frankenstein. I suggest, therefore, that individuals with the type of mind which is capable of proceeding from the special and particular to the general and more universal, will do well to face their future before they have become cramped by their environment. I shrewdly suspect that the men who will guide the future of medical practice most wisely will not rarely be found among the group who have mastered some field in their earlier years but have felt the compression of their environment, have recognized, or had recognized for them, their capacity to become generalists rather than specialists, and have gone on from their mastery of a narrow field to a comprehension of a much larger whole. Thus in our planning for the future it is conceivable that we shall find the men capable of wisely grasping the larger implications of medical practice among those who have at least some comprehension of what the word mastery means.

REGISTRATION OF SPECIALISTS

As I have already suggested, we have for more than two generations been vividly aware of some of the dangers inherent in specialization. We have recognized the fact that not only for the benefit of the public but for that of the profession, there must be some way of distinguishing between the real article and a shoddy substitute. Until relatively recent times, we have been more or less content to acquiesce in the view that a physician was a specialist, based frequently upon his own assertion and not upon any recorded evidence. Recently there has been set up under the auspices of the American Medical Association special boards for the examination and indication of those members of the profession who give evidence of having had adequate special training in their fields. Such boards may be looked upon as having two purposes; one, that of insuring reasonable qualifications for those who desire to label themselves as specialists, and two—which is perhaps more important—the setting up of some method by which a bewildered public can identify men having the confidence of their colleagues and distinguish them from those whose special training has been insufficient.

GENITO-URINARY SURGERY. UROLOGY

Specialization in this field has come about in this country chiefly during the present century. Prior to that time, though there were many outstanding figures best known for their work in this field, these men were not specialists in the sense that they thus limited their practice, nor were they specialists in the sense that they had had what we should not regard as adequate special training because forsooth there was nowhere that they could have obtained this training. They were either what we now call internists or general surgeons, sometimes even what we might now call general practitioners. In this group one may think of Van Buren, Gouley, Fessenden Otis, Keyes, White (of Philadelphia), Bryson and Mudd (of St. Louis), Belfield (of Chicago), Chismore (of San Francisco), Bigelow, Watson, and A. T. Cabot (of Boston), and many others. The contributions of this group were great but they were not the contributions of specialists. The only specialists at all approaching this field were in fact not genito-urinary surgeons or urologists but venerologists. Fortunately for the future, the temper of the time did not look kindly upon the development of venerology as a specialty. I say fortunately because I think those who remember this rather small group, at least in this country, will have been impressed by the fact that the confinement of their practice to this field was very likely to react unfavorably upon their character. It would take a personality of unusual force to resist the warping and confining effects of prolonged contact with such a type of patient.

We may perhaps date the beginning of specialization in genito-urinary surgery here from the organization of the American Association of Genito-urinary Surgeons in 1886. Perhaps we may also date the introduction into this field of the term urologist from the organization of the American Urological Association in 1902. Precisely how the term urologist sprang up is to me obscure. It was, I think, imported from foreign lands. It is just possible that it had its origin in the prudish desire to cast a taint of respectability over a field which was at that time more or less taboo. Whether or not the term urologist suggesting, if it suggests anything, that the expert confines his machinations to diseases of the urinary tract, was a desirable change in terminology I am not clear. Certain it is that it less clearly defines the field, and I am not sure that it has not laid the foundation for certain difficulties with which our successors will have to struggle. We may even be put to it today to answer the question, what is a urologist? If one surveys the fields lightheartedly, one might almost conclude that it varied with other scientific possibilities from nothing to infinity. There are urologists today who confine their work to such a microscopic field that it may almost be said to center in the lens of the cystoscope. At the other extreme we find men who, soundly trained in general surgery, have gradually dropped off one field of endeavor after another until they now confine themselves to the surgery of the genito-urinary apparatus. Such men, though often very able and dexterous surgeons, are likely to be undistinguished diagnosticians and are in danger of confusing surgery with the doing of surgical operations.

All of this is but a long way of saying that there is a good deal of confusion among the group now loosely referred to as urologists. The general surgeon complains that the urologist is not properly trained in the underlying and essential field of general surgery. He points out that though the urologist may be an exceedingly expert diagnostician, he is often not well equipped to carry out his own prescriptions, which may require great niceties of judgment and great ability to deal with unexpected operative emergencies. On the other hand, the urologist complains—and properly—that the general surgeon is likely to operate upon the basis of a diagnosis made by somebody else with the details of which he

is unfamiliar, that he could not himself carry out the necessary diagnostic procedures and is, therefore, not a sound judge of their accuracy or completeness. The fact of the matter is that both groups are right. Some urologists are not properly qualified surgeons. Some genito-urinary surgeons are not properly qualified diagnosticians.

Now it is just possible that a part of this dilemma has arisen from our lighthearted attempt to conceal our identity under the term urologist in the hope of attaining respectability. There are times when I congratulate myself that I am not concerned with the labors of the American Board of Urology. They will have willy nilly to separate the sheep from the goats. They will have to decide whether the cystoscopist and the diagnostician is to be declared a urologist and whether the dexterous operating surgeon whose brilliancy sometimes befogs his judgment is to be placed in the same classification. They may even find the dilemma insoluble. They may have to agree that the weakness of the term urologist has come home to roost and that they are being hoisted with their own petard. It seems to me now inconceivable that they may have to subdivide the field and distinguish between the qualified genito-urinary surgeon on the one hand and the qualified urological diagnostician on the other. And here I will leave them to their discussions, which will doubtless be acrimonious, and to their even more inevitable headaches.

Hugh Cabot.

REFERENCE

1. Cabot, Hugh. Specialization in medicine: A subject for undergraduate planning. *New England J. M.*, 217: 24–27 (July) 1937.

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ORIGINAL ARTICLES

THE RELATION OF WATER, SODIUM CHLORIDE, AND ACID-BASE BALANCE TO RENAL FUNCTION IN THE TREATMENT OF LESIONS OF THE URINARY TRACT

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THE preservation and maintenance of adequate renal function is one of the most important considerations in the management of patients suffering from diseases of the urinary tract. It is important to remind the reader at the outset that the functional disorders of the kidney which are commonly seen by the urologist, and which are often called "surgical" diseases of the kidney, present an entirely different problem as to etiology, pathology, treatment, and prognosis than does the so-called medical nephritis which may for the sake of simplicity be grouped under the broad term of "glomerular nephritis." A discussion of the latter type of renal pathology, however, is not within the scope of this paper except in so far as we may briefly compare the two types of renal disease.

Renal insufficiency of the surgical type, as seen by the urologist, is in the majority of cases the result of urinary obstruction, either unilateral or bilateral, and it is often complicated by secondary infection. Exceptions to this general rule are occasionally encountered in the case of older patients whose arteriosclerosis has produced the so-called arteriosclerotic kidney, which in turn has resulted in varying degrees of renal insufficiency. In general, however, the "surgical" disease is locally confined and is not characterized by generalized vascular disorders such as are commonly seen in cases of glomerular ("medical") nephritis. Renal disorders of the surgical type do not cause hypertension or retinitis; in glomerular nephritis, on the other hand, hypertension and retinal changes are the rule. Since renal insufficiency in surgical nephritis is so commonly caused by obstruction, the lesion becomes a mechanical one and results in dilatation of the ureters, pelvis, and calices, with secondary injury and destruction of the glomeruli and tubules. Relief of the obstruction and infection is commonly associated with a reversal of this process, with resultant improvement in renal function. On the other hand, since the lesions of glomerular nephritis are associated with vascular disturbance of the kidneys and vascular changes generally, the process is usually a progressive one. The prognosis in the two types of renal disease is therefore obvious.

The management of these two types of renal disease offers varying problems which are in many respects entirely different. For example, in certain stages of glomerular nephritis, because of the difficulties of water and electrolyte excretion, as well as the fact that plasma proteins are frequently reduced, varying degrees of edema are frequently encountered. The excretion of water in surgical diseases of the kidney rarely becomes a serious problem except when edema is "man-made." The term "uremia" is misleading. Patients suffering from surgical diseases of the kidney are frequently found to have an extreme degree of azotemia and a blood urea as high as

200 to 300 mg. per 100 cc. with apparently no constitutional ill effects. "Uremic" convulsions are rarely seen in this group of patients. That convulsions of this type are not due to elevation of the blood urea alone is a well-known fact, and that the convulsions seen in various types of medical nephritis are the result not only of renal insufficiency, but also of secondary vascular changes, especially in the brain, plus alterations in the chemistry of the blood plasma, seems quite well established.

Hypertension is neither caused by nor is it the result of renal insufficiency in the surgical types of renal disease. While some elevation of the blood pressure is not infrequently seen in patients during the acute phases of urinary obstruction (as for example in those suffering from prostatic hyperplasia), with relief of the obstruction the blood pressure usually returns to a level which was "normal" for that patient. Patients suffering from prolonged urinary obstruction due to prostatic enlargement, who have varying degrees of renal insufficiency, do not have a higher blood pressure than a similar group of the same age who have not had urinary obstruction. On the other hand, hypertension is the rule among patients with glomerular nephritis.

The more recent advances in our knowledge of the physiology of the kidney have helped us to realize that the maintenance and improvement of renal function is intimately associated not only with the excretory function of the kidney, but also with its non-excretory functions. For normal functioning of the kidney a normal composition of the blood plasma is necessary. Alterations in various components of the plasma may seriously damage renal function or may retard improvement in renal function. These are some of the problems which we propose to consider. In order that these problems may be thoroughly understood, a working knowledge of the physiology of the kidney is necessary:

PHYSIOLOGY OF THE KIDNEY

The complex structure of the kidney and the many difficulties encountered in the investigation of its individual units have interested physiologists for almost a century. It is not necessary to mention the controversies that raged between Bowman (1843) and Ludwig (1844) and later Heidenhain (1874). While even today there is no complete agreement among physiologists as to all the details of renal physiology, sufficient evidence has accumulated to form a reasonably satisfactory working basis. For obvious reasons, it has been practically impossible to carry out physiologic experiments on human subjects and most of the work has of necessity been done on the amphibian kidney. It may, of course, be questioned whether the results of experiments on the kidneys of frogs and Necturus (water salamander) can be applied to the more complicated structure of mammalian kidneys. However, as the amphibian kidney closely resembles the mammalian kidney, one may assume that the functions of the two are similar.

While in a study of the physiology of the kidney it is necessary to consider the glomeruli and tubules as individual units, one must not lose sight of the fact that the interrelation of these structures which act as a unit and preserve the chemical composition of the blood plasma to a minute degree, is from the practical standpoint of the utmost importance. It is now generally agreed that the watery fluid which leaves the glomeruli and enters the tubules is identical in composition with the blood plasma, *minus the protein*. It is also believed that this fluid passes out of the blood through the glomeruli by a process of simple filtration. Probably the most convincing proof of this was presented by the ingenious work of Wearn and Richards.[19,20] They were able to puncture the glomeruli of the living, American giant frog by means of a fine capillary pipet, and to obtain directly some of this glomerular fluid. The fluid was found to be protein-free, and

neutral in reaction, although it was slightly on the alkaline side. Quantitative studies of this fluid have shown that it has the same content of chloride, glucose, urea, uric acid, inorganic phosphates and creatine as the blood plasma. The molecular content and the phosphates are the same in both fluids. In other words, it was shown that the capsular fluid was qualitatively and quantitatively similar to a plasma ultrafiltrate. It would seem, then, that because the glomerular filtrate is identical with the protein-free ultrafiltrate of the blood plasma, the formation of glomerular fluid must depend upon a process of simple physical filtration.

The blood pressure as a factor in the rate of elimination of urine may be taken as an established fact. Without discussing all of the experimental evidence, it may be stated that Hayman,[11] and later White,[21] have shown that in frogs whose aortic pressure measures 37 cm. of water, an average pressure of 20.2 cm. of water is found in the capillaries of the glomerulus. The glomerular pressure is thus approximately 54 per cent of the aortic pressure. When these figures are applied to the mammalian kidney, it appears that the secretion of the kidney stops when the aortic pressure goes down to from 50 to 60 mm. of mercury. Under these circumstances the hydrostatic pressure in the capillaries of the kidney must vary from 27 to 32 mm. of mercury (that is, 54 per cent of 50–60 mm.). Thus urine is excreted only so long as the hydrostatic pressure in the capillaries of the glomeruli exceeds the colloid osmotic pressure of the proteins of the plasma, which in man amounts to about 30 mm. of mercury. When the hydrostatic pressure in the glomerular loops is lowered to a value equal to or lower than the colloid osmotic pressure of the plasma, the secretion of urine stops. The views held by the older physiologists on autochthonous variations in intraglomerular pressure seem to have been exact, because an increase in the blood pressure in the aorta produced by injections of epinephrine has no influence on the velocity of the blood stream through the kidney.

The permeability of the glomerular membrane can be compared with that of a collodion membrane. Bayliss, Kerridge, and Russell[1] have shown that proteins with a high molecular weight, that is, with large molecules, like albumin (molecular weight 67,500), globulin (103,800), and casein (188,000), were never excreted by the perfused kidney, whereas, proteins with smaller molecules, like gelatin (35,000), egg white (34,500), and Bence Jones protein (35,000), were readily excreted by the perfused kidney. Hemoglobin, which has a molecular weight of 68,000, was excreted only if the concentration in the serum exceeded a certain threshold value. The glomerular membrane evidently works as a filter whose pores are permeable to crystalloids and to colloids with a molecular weight below ±60,000. All these factors give wide credence to the generally accepted theory of glomerular filtration.

If one accepts the theory of glomerular filtration, one must then assume that absorption takes place in the tubules. The work of Wearn and Richards again proved conclusively that this is the case. For instance, glucose could readily be demonstrated in the glomerular fluid of the frog but none could be found in the vesical urine; and it, therefore, must have been absorbed during its passage through the tubules. The same was true of chlorides. Glucose has been shown to be reabsorbed in the proximal convoluted tubules, chlorides in the distal convoluted tubules, and water in both parts of the tubule, although more in the distal portions.[16] In the human kidney, substances like glucose are for the most part completely reabsorbed. Chlorides and water are reabsorbed to supply bodily needs; other substances are reabsorbed in varying quantities.

If one studies the behavior of urea, an idea can be obtained as to what the kidney does in the way of the reabsorption of water in the tubule. The normal daily excretion of urea is approximately 30 gm. Normal blood urea averages 0.03 per cent, or 30 gm. per 100 liters of plasma. Thus about 100

liters of plasma filtrate would have to filter out of the glomeruli in twenty-four hours. As there is an average output of 1.5 liters of urine a day, 98.5 liters of water must be reabsorbed by the tubules. Whether or not the tubule secretes certain substances, thereby adding to the urine certain of its component parts, is still a matter of contention. The weight of experimental evidence, however, seems to favor tubular secretion as well as absorption.

WATER BALANCE

The physiologic data just cited give one some insight into the very complicated functions carried on by the kidney in the excretion of urine. The maintenance of a proper water balance, that is, an adequate intake and output of fluid, is one of the most important factors in helping the kidney bring this about.

The amount of fluid required to maintain a normal water balance depends to a large extent, of course, on the amount of fluid lost and there should be a sufficient amount to compensate for dehydration when present. Coller and Maddock[4] have shown that the amount of water necessary for a sick surgical patient, to provide for his daily water excretions, is as follows: (1) water for vaporization, 2000 cc.; (2) water for urine, 1500 cc., and (3) for abnormal loss in vomitus, diarrhea and so forth, up to a total of 3500 cc. When patients are dehydrated, an intake of fluid of 7000 cc. is frequently necessary in order to return the patient to a normal water balance. It is obvious, of course, that fever and chills which result in a large loss through the skin, as well as climatic conditions, must be taken into consideration. The amount of renal damage must also be taken into consideration in deciding on the amount of fluid to be used. There is less danger in giving a slight excess of fluid, provided it is properly eliminated, than in giving too little fluid.

Lashmet and Newburgh[13] have shown that individuals whose kidneys are damaged are unable to form as concentrated a urine as a normal person. This necessarily means that the urine of the former has a high water-total solid ratio. The lower the concentrating ability or the more renal damage that is present, the greater must be the volume of urine in order to improve or prevent the retention of waste products. In renal disease, the body tends to avoid the retention of waste products by increasing the output of water, in compensation for the low concentrating ability of the kidneys. Thus if the intake of water is too low, body water may be released. If, however, body water is not released or cannot be released because, for example, of an excessive intake of sodium chloride or a diminished serum protein level, then the process fails and the piling up of waste products results.

EDEMA AND THE ADMINISTRATION OF SODIUM CHLORIDE

Fortunately the development of edema in patients with surgical diseases of the kidney is comparatively rare except, as has been suggested, as it may be allowed to develop through improper management. The development of edema among postoperative surgical patients whose convalescence has been slow, who have suffered from prolonged fever, and who have received daily intravenous injections of saline solution, is a matter of common observation. In the case of the average surgical patient the intravenous injection of saline solution is not carried out for more than two or three days, so that the development of edema is rarely encountered; if it is present, it will not appear in the legs, where edema is usually encountered, but will be seen by turning the patient so that his back can be inspected. With the resumption of fluids by mouth, what edema has developed promptly disappears.

The amount of edema is usually directly related to the length of time the patient receives the intravenous injections of saline solution. Coller, Dick and Maddock[5] have recently called attention to this fact. They found that twelve of the thirteen

surgical patients who had received 5 per cent dextrose in physiologic saline or Ringer's solution gained weight as a result of retained fluids. Ringer's solution was slightly less likely to cause retention of fluid than was physiologic saline solution. On the other hand, no fluid was retained by a group of surgical patients who were given 5 per cent dextrose solution in distilled water. Furthermore, in those cases in which edema developed as the result of the excessive administration of sodium chloride, the use of the dextrose was shown to be very effective in the elimination of retained fluids.

The concentration of sodium chloride in the blood plasma has no direct relation to the amount of edema present. In fact the plasma content of chlorides may sometimes be below normal in the presence of edema. The tissues, however, will be found to have an increased salt content. Normally the intake of sodium chloride is between 6 and 10 gm. a day, an equal amount being excreted in the urine. If the use of salt has been restricted, the body will retain a sufficient amount to comply with its needs; in cases of renal insufficiency, however, the excretion of salt is interfered with and salt may accumulate in the tissues. The same is true of an excessive intake of salt, in which case the kidneys are unable to eliminate the salt as fast as it is given. For example, each liter of physiologic saline solution contains 8.5 gm. of sodium chloride and, when 5000 cc. of this solution is given in twenty-four hours, the patient would be given 42.5 gm. of salt. This is certainly an amount much in excess of what the average patient needs and probably in excess of what he can eliminate day after day.

Fantus[8] has described a simple test for studying the sodium chloride output in the urine which should be a valuable rough guide in determining what the salt requirements of the patient are. The test is as follows: "Place 10 drops of urine in a test tube, add 1 drop of a 1:5 potassium chromate solution. The fluid will now assume a somewhat distinctly yellow color. Add drop by drop with the same dropper or one of the same caliber 2.9 per cent silver nitrate solution until a permanent and distinct color change to red-brown occurs (resulting from the formation of silver chromate). The number of drops required to produce change of color expresses in grams the content of chloride per liter of urine."

Unfortunately no strict rule can be laid down for the administration of salt. Each case must be individualized. The loss of salt through the skin by sweating during fevers and in hot weather must be considered. The amount of salt excreted in the urine must be known as well as the level of chlorides in the blood plasma. The patients studied by Coller and his associates had no evidence of renal disease. Thus if edema develops so easily in patients without renal diseases as the result of the excessive injection of saline solutions, edema would be more easily produced in patients with renal disease, as there is a definite relation between the ability to excrete salt and renal insufficiency. On the other hand, the fact must be emphasized that the plasma chlorides must be normal, for to have normal renal function sufficient chlorides must be present in the blood plasma. An excessive chloride content of the blood plasma may also damage renal function.

Whether or not the development of a small amount of edema is harmful to the patient is not definitely known. More than likely short periods of edema are not harmful, but as Fantus has said, the sicker the patient is the more fluid he usually gets, and certainly the finding of water-logged tissues at necropsy would indicate that such treatment had not been to the best advantage of the patient.

INTRAVENOUS INJECTIONS OF FLUID

One of the most significant advances in modern medicine has been the development of methods of supplying, intravenously, fluids, food and other chemicals to patients whose gastro-intestinal tract has been upset or who for some other reason need parenteral fluids. Whether or not this has been

an unmixed blessing should be a subject for contemplation. Certainly as far as the comfort of the patient is concerned the advantages of the intravenous administration of fluids over hyperdermoclysis cannot be doubted. But that the patient has gained comfort and sacrificed safety by the injudicious use of a dangerous instrument in the hands of the unskilled cannot be denied, and while the skilled use of intravenous solutions in proper amounts and composition is not infrequently a life-saving measure, the improper use of such solutions may certainly at times do the patient harm.

In the last few years, since intravenous solutions have been properly prepared and the "reaction" following the injection is largely a thing of the past, some have literally pumped barrels of fluid into patients without knowing exactly how much good or harm was being done. Fantus has called attention to this state of affairs, but as yet no one has come forth with the answer. The reader is respectfully referred to his article which contains much food for thought.

The amount of fluid necessary, the type of fluid, and the rate of injection have all been the subject of much controversy and experimentation. Cutter,[6] from a study of the output of a laboratory making commercial intravenous solutions, found that 5 per cent dextrose in physiologic saline solution was most commonly used, this mixture comprising 36 per cent of intravenous solutions. Ten per cent glucose in physiologic saline solution was second and physiologic saline solution was third in popularity. The most interesting figures presented, however, were those which dealt with the sectional use of intravenous fluids. For example, in the Northwest 62 per cent of the solutions used were 5 per cent glucose in physiologic saline solution, whereas in the Southwest, this solution was used in only 14 per cent of cases. This would certainly indicate that, as yet, there was no uniformity of opinion as to what solution was best to use.

In the earlier use of fluids intravenously reactions seemed to follow injections of glucose solutions more commonly than those of saline solutions, and it may be that this is a reason why glucose solutions have not been as commonly used as saline solutions. At the present time, however, reactions occur so rarely as to be negligible, and they are perhaps the least of the harmful effects of the intravenous administration of fluids.

Dextrose, on the other hand, has the added advantage of acting as a protective mechanism. When little or no food is taken by mouth, the glycogen content of the body is rapidly diminished and fat, which then becomes the main source of energy, is incompletely oxidized, with a resultant ketosis caused by the formation of beta oxybutyric and diacetic acid. Glucose also acts as a definite protective medium for the liver. The caloric value of glucose is not inconsiderable; for example, 1500 cc. of 10 per cent glucose provides 600 calories. There is an accumulating amount of evidence that glucose solutions in somewhat higher concentrations have a beneficial effect in cases of the more acute coronary disturbances. It is possible that the use of glucose solution might in such cases also have a protective influence.

The administration of glucose intravenously is not infrequently followed by the appearance of varying amounts of sugar in the urine. This has never seemed, in our experience, to be of any significance in the case of the non-diabetic patient, although it demands at least a certain amount of consideration. Woodyatt, Sansum, and Wilder[22] found the average glucose tolerance of patients receiving continuous intravenous injections of dextrose to be 0.8–0.9 gm. per kg. of body weight per hour. A man weighing 70 kg. should therefore be capable of tolerating 1512 gm. of glucose in twenty-four hours. Fantus, however, held that this calculation does not apply to the manner in which most intravenous fluids are given. In his series, when 100 to 149 gm. of glucose were

given in twenty-four hours about a third of the patients showed glycosuria. The number of patients with glycosuria of course increased as larger amounts of glucose were given. Fantus drew no conclusion from his study, but found that the mortality increased greatly when the intake of 100 gm. of glucose in twenty-four hours was exceeded. Furthermore it must be remembered that 20 cc. of fluid are required for every gram of sugar passed in the urine, a fact requiring consideration in the case of the dehydrated patient.

When sugar solutions are to be used, in general, a 5 per cent solution of glucose in distilled water is the solution of choice. Solutions with high concentrations of dextrose should be used only when specifically indicated. Ten per cent glucose solutions are sometimes used when mobilization of edema is indicated; higher concentrations are used most commonly in the treatment of other conditions. The higher the concentration of an intravenous glucose solution, the greater the likelihood is there of venous thrombosis at the site of injection—a fact that becomes very important when intravenous injections are indicated daily over a long period of time. Certain other factors must be taken into consideration in the selection of a fluid for intravenous use in cases of renal insufficiency. The most important of these is regulation of the acid-base equilibrium and the serum protein content of the blood. These matters will be discussed subsequently.

There are certain extrarenal conditions causing renal insufficiency which also demand consideration. The most important of these is that associated with loss of fluids from the upper part of the intestinal tract such as is seen in cases of pyloric obstruction and prolonged vomiting. Attention was first called to this condition in 1922 by Tucker,[18] and in 1923 by Brown, Eusterman, Hartman and Rowntree.[3] The condition is characterized by loss of fluids, chlorides and acid, which explains the hypochloremia and alkalosis. Studies of renal function reveal an increased urea content of the blood, a diminished phenolsulphonthalein output, albuminuria and cylindruria. Inability to cope with this situation frequently leads to progressive toxemia, renal insufficiency and death. Treatment consists in the administration of fluids and chlorides in the form of physiologic saline solution and in relief of the etiologic factor.

SERUM PROTEIN

A diminution in the plasma proteins is likewise a factor in the production of edema, and while in our experience this complication has been uncommon in dealing with patients with urologic disorders, it does occasionally occur and it must accordingly be kept in mind. Lowered plasma protein is sometimes a complication of anorexia, malnutrition, or prolonged suppurative drainage. Severe albuminuria is an uncommon finding in surgical diseases of the kidney so that loss of protein in this manner is not common. As mentioned under physiology of the kidney, the osmotic pressure of the serum protein in mammals is approximately 30 mm. of mercury. This pressure has to be exceeded or there is no filtration of water and solids by the kidney. A compensatory mechanism at times comes into play, however, for when the plasma proteins are reduced a pressure of 18 mm. will suffice.

Epstein[7] has stated that the normal protein content of the serum is from 6.5 to 8.5 gm. per 100 c.c. The blood proteins are composed mainly of albumin and globulin, the normal ratio of albumin to globulin in the serum being about 2:1. Approximately 85 to 90 per cent of urinary protein is albumin; the remainder is globulin. Thus since more albumin than globulin is lost from the blood, there frequently develops a reversal of the albumin-globulin ratio. Bell[2] stated that the loss of plasma albumin lowers the osmotic pressure much more than the loss of a corresponding percentage of globulin, since the molecules of albumin are much smaller than those of globulin (the molecular weight of globulin being

103,800, that of albumin 67,500). Moore and Van Slyke[15] have shown that when the serum protein drops to 5.5 ± 0.3 gm. per 100 cc., fluid leaves the blood and goes into the tissues. The serum albumin, however, has to fall below a level of 2.5 ± 0.2 gm. per 100 cc. before edema occurs.

Jones and Eaton,[12] in their study of post-operative edema, found that edema may occur as early as the day of operation but that it usually appears from two to fifteen days post-operatively. They again emphasized the fact that the edema is usually found in the dependent portions of the body, and when the patient is in bed that means the back. The edema was found to be inversely proportional to the level of the serum protein and somewhat less consistently proportional to the level of the serum albumin. They also emphasized the fact that the average patient received post-operatively three times the average normal intake of salt, which was a further factor contributing to the development of edema. Hypoproteinemia may sometimes be benefitted by blood transfusion or by the administration of 500 cc. of a 6 per cent solution of acacia.

ACID-BASE REGULATION

Finally, the regulation of a normal acid-base mechanism in the body is an extremely important factor in the maintenance and improvement of renal function. Here again it should be emphasized that a normal composition of the blood plasma is necessary for normal renal function. Alkalosis frequently accompanies renal insufficiency and of itself has a deleterious effect upon renal function; the reverse situation, acidosis, not infrequently also impairs renal function. This latter fact must be remembered in the management of infections of the urinary tract when ammonium chloride, ammonium nitrate, calcium chloride and the ketogenic diet are employed. While these substances frequently exert a markedly beneficial effect on cystitis and pyelitis as well as on cardiovascular and portal failure when employed therapeutically, renal function must be controlled, and this is especially true in the presence of renal insufficiency.

The complicated mechanism whereby the body maintains an accurate acid-base equilibrium will not be discussed here. The reader who is interested in the details of this process is referred to a recent article by Snapper.[17] It may be said, however, that in renal insufficiency one of the important non-excretory functions of the kidneys is seriously interfered with—namely, the ability of the kidney to manufacture ammonia. This results in the production of acidosis, and it is probably the most important factor in the causation of the acidosis so commonly seen in renal insufficiency. The degree of acidosis (or alkalosis) may be determined by studying the carbon-dioxide combining power of the blood plasma.

The treatment of the acidosis of renal insufficiency plays an important part in bringing about improvement in renal function. Sodium bicarbonate, in the form of a 5 per cent solution and in quantities of from 100 to 500 cc. intravenously, has been commonly used and would seem to be an ideal solution for this purpose. Certain precautions, however, must be taken: Since the solution is strongly alkaline, the effect produced is prompt and rapid and it may very easily change an acidosis into an alkalosis. The following is a case in point:

Case 1. A man, aged 84 years, had had symptoms of increasing urinary obstruction for three years. Finally, he was entirely unable to void and he had to be catheterized. He had been vomiting frequently. On admission to the hospital on Jan. 5, 1937, he was markedly dehydrated, very weak and stuporous. His prostate gland was enlarged, grade 4, the enlargement being due to benign hyperplasia. He was given 2000 c.c. of physiologic saline solution immediately on admission after an inlying urethral catheter had been inserted. (Table 1.) Physiologic saline solution was used in this case because it was assumed that since the patient had been vomiting, his blood chlorides might be reduced. This was subsequently found not to be the case. The elevated blood chlorides in this instance may have been

related to the factor of dehydration. The use of physiologic saline solutions intravenously in cases of dehydration may have a beneficial effect in aiding the body to retain fluids until a satisfactory water balance has been established. A study of the carbon-dioxide combining power of the blood showed the presence of definite acidosis. This was combatted by the use of 500 cc. of a 5 per cent solution of sodium bicarbonate. As the acidosis was quite marked, it was considered that a second injection would be necessary; this was carried out before the results of the studies of blood chemistry were known, with a resultant alkalosis as indicated by a carbon-dioxide power of 80.6 volumes per 100 cc.

TABLE I

BLOOD FINDINGS AND INTRAVENOUS MEDICATION, IN A CASE OF URINARY OBSTRUCTION, SHOWING EFFECT OF ADMINISTERING SODIUM BICARBONATE INTRAVENOUSLY

(Case 1)

January	6	7	8	9	10	11	12	13	14	15
Urea (mg./100 cc.)	174	....	90	.....	....	....	48	....	....	48
Creatinine (mg./100 cc.)	2.2	....	1.5							
Chloride (mg./100 cc.)	651	....	600	.....	....	....	.....	....	....	558
Carbon dioxide combining power (vols./100 cc.)	21.1	....	57.9	80.6	....	....	66.4	....	....	55.1
Intravenous Medication										
Physiologic saline solution (cc.)	2000	....	.....	.....	....	....	.....	2000	2000	1000
5% glucose in distilled water (cc.)	.....	1000	1000	1000	1000	1000	1000	....	....	1000
5% sodium bicarbonate (cc.)	.....	500	500							

While this patient suffered no ill effects and improved daily, the case is cited to illustrate the necessity for caution and the importance of frequent studies of the blood chemistry when sodium bicarbonate is used intravenously. One injection of 500 cc. of a 5 per cent solution of sodium bicarbonate in this instance would have been sufficient to combat the acidosis. In general, not more than one injection of the solution should be given without studying the carbon-dioxide combining power of the blood.

In the treatment of acidosis, Hartmann and his associates[9,10] have advocated the use of a solution of sodium lactate. The advantages of this solution, according to Moore,[14] are: (1) it is completely metabolized, liberating sodium quantitatively; (2) the effect occurs rapidly, but not rapidly enough to produce alkalosis easily; (3) it is easily prepared and is stable; and (4) it is non-irritating in the concentration used and may be given intravenously, intraperitoneally, or subcutaneously. Keiter stated that 60 cc. of a ⅙ molar solution per kg. of body weight will increase the carbon dioxide combining power of the blood by about 35 per cent. The following solution, which is Hartmann's modification of Ringer's solution, has been found most satisfactory when acidosis is present secondary to renal insufficiency, especially in cases in which patients are dehydrated and in which sodium chloride is indicated: sodium lactate, 2.4 cc. (60 to 70 per cent); sodium chloride, 6.0 gm.; potassium chloride, 0.4 gm.; calcium chloride, 0.2 gm., and water q.s., 1000 cc. This solution has the advantage of adding certain electrolytes which are sometimes found to be deficient in the blood plasma.

The following cases indicate the effectiveness of this solution in combating acidosis associated with renal insufficiency:

Case II. A man, aged 69 years, was admitted to the hospital on March 31, 1937, with a history of urinary frequency, nocturia, and dribbling of several months' duration. He seemed in excellent general condition, however, and had no complaints except those related to the urinary system. Physical examination

revealed evidence of moderate dehydration and benign prostatic enlargement, grade 2. The residual urine measured 200 cc. The blood chemistry studies and intravenous medication are indicated in Table II.

and abdominal palpation revealed the bladder to be distended to the level of the umbilicus. The prostate gland was enlarged, grade 4. Since the patient had found that the more fluid he drank the more difficulty he had in voiding,

TABLE II

BLOOD FINDINGS AND INTRAVENOUS MEDICATION, SHOWING EFFECTIVENESS OF HARTMANN'S SOLUTION IN COMBATING ACIDOSIS ASSOCIATED WITH RENAL INSUFFICIENCY

(Case II)

April	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Urea (mg./100 cc.)	238	....	.....	129	....	....	98	....	....	84	....	....	80	....	....	....	66
Chlorides (mg./100 cc.)	....	....	627	664													
Carbon dioxide combining power (vols./100 cc.)	....	....	35.3	40.5	....	....	42.8	....	....	.....	....	....	46.6				
Creatinine(mg./100 cc.)	8	....	.....	4.2	....	....	3.6	....	....	3.6							
Intravenous Medication																	
Physiologic saline solution (cc.)	2000	2000	2000														
5% glucose in distilled water (cc.)	....	....	.....	1000	1000	1000	1000	1000									
Hartmann's solution	....	....	.....	1000	1000	1000	1000	1000	2000	2000							

TABLE III

BLOOD FINDINGS AND INTRAVENOUS MEDICATION, SHOWING EFFECTIVENESS OF HARTMANN'S SOLUTION IN COMBATING ACIDOSIS ASSOCIATED WITH RENAL INSUFFICIENCY

(Case III)

	March						April					
	22	23	24	25	26	27	1	3	4	5	6	7
Urea (mg./100 cc.)	249	....	....	....	....	222	243	.....	....	.....	....	189
Creatinine (mg./100 cc.)	11.2	....	....	....	....	8.4	7.2	.....	....	.....	....	7.2
Sulphate (mg./100 cc.)	21.4	....	....	....	....	.....	19.2					
Chlorides (mg./100 cc.)	.....	....	....	....	....	553						
Carbon dioxide combining power (vols./100 cc.)	37.2	....	....	....	....	21.1	28.7	28.7	....	35.2	....	40.9
Intravenous Medication												
Physiologic saline solution (cc.)	1000	2000	2000	2000								
5% glucose in distilled water (cc.)	.....	....	....	....	2000	1000						
Hartmann's solution	.....	....	....	....	....	.....	1000	1000	1000	1000	2000	2000

Case III. A man, aged 68 years, was admitted to the hospital on March 22, 1937, with the history of frequency, nocturia, small urinary stream and slowness in starting urination of fifteen years' duration. He had been able to void only a few drops of urine at a time,

his intake of fluid had been markedly reduced with a resultant severe dehydration which had been augmented by a moderate amount of vomiting. The residual urine measured 750 c.c. The blood chemistry studies and the intravenous solutions used are indicated in Table III.

It is of interest to note in Case 11 that, in spite of the marked renal insufficiency, as evidenced by a blood urea of 238 mg. per 100 cc., the patient was in excellent general condition. He presented none of the usual symptoms of renal insufficiency. He was first given intravenous injections of physiologic saline solution, but as soon as it was apparent that the plasma chlorides were somewhat above normal limits, administration of this solution was discontinued and 5 per cent glucose in distilled water and Hartmann's solution were substituted. It will be noted that in spite of the low carbon dioxide combining power of the blood plasma there were no clinical symptoms of acidosis. Furthermore it will be observed in all these cases that as the carbon dioxide combining power of the blood approached normal there was a corresponding improvement in renal function, as evidenced by decreasing urea content of the blood plasma. It is not likely that this factor alone is responsible for the improvement in renal function. Certainly, drainage of the bladder and the administration of large quantities of fluid both intravenously and by mouth in addition to combating acidosis are all-important factors in the management of this type of renal insufficiency.

SUMMARY AND CONCLUSIONS

The preservation and maintenance of adequate renal function is one of the most important considerations in the management of patients with lesions of the urinary tract. Functional disorders of the kidney associated with diseases of the urinary tract, which are often called "surgical" diseases of the kidney, differ from so-called medical nephritis in etiology, pathology, treatment and prognosis. Hypertension and arteriosclerosis are not directly related to surgical diseases of the kidney as is so often the case in glomerular nephritis.

Alterations in various components of the blood plasma may seriously affect renal function and retard improvement in renal function. A knowledge of the physiologic mechanism of renal function is essential.

The maintenance of a proper water balance is one of the most important factors in aiding the kidney in carrying out its complete function, and the modern use of intravenous fluids is one of the significant advances in medicine. That this method of supplying fluids parenterally is at times a life saving measure cannot be doubted. There does not seem to be, however, a uniformity of opinion at the present time as to the amount and composition of intravenous solutions which should be used in various conditions.

Edema is not a common complication in surgical diseases of the kidney, but it may develop as the result of the excessive intake of fluids, especially saline solution. The use of 5 per cent dextrose solution intravenously is probably preferable when fluids are to be given parenterally, unless there is a specific indication for other types of fluid.

The extrarenal causes of renal insufficiency, such as the toxemia associated with prolonged vomiting and obstructive lesions in the upper part of the gastro-intestinal tract play an important rôle in dealing with patients suffering from postoperative complications. Their rôle in renal insufficiency must be considered.

Lowering of the plasma proteins may occasionally, when associated with malnutrition, anorexia, and suppurative drainage, be one of the factors in the production of edema.

The acid-base regulation of the blood plasma is an important function in maintaining or improving renal function. One of the non-excretory functions of the kidney is the manufacture of ammonia. This mechanism is disturbed in renal insufficiency, resulting in acidosis. The treatment of acidosis associated with renal insufficiency by the use of intravenous alkalies, sodium lactate and Hartmann's solution is discussed.

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ASCENDING INFECTION OF THE URINARY PASSAGES*

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THIS discussion is not to be controversial, concerning the likelihood of ascending or hematogenous infection, but it is to point out, first, the evidence there is for believing that infection occurs by the ascending route, and second, to point out its most likely course in ascending.

In ascending infection of the kidney there are three distinct problems to consider: the mode of infection of the bladder; the mode of infection of the pelvis of the kidney; and the mode of infection of the renal parenchyma, the kidney proper. By considering these three steps separately, I think physicians are much more likely to come to an agreement as to the route of ascent.

INFECTION OF THE BLADDER

With regard to bacillary infections, the question arises as to whether the infection reaches the bladder by way of the kidney, the lymph channels, or the urethra. I am not considering the coccal infections because they make up a relatively small percentage of the total and it can be assumed that, with the exception of the Streptococcus faecalis, most of the cocci reach the urinary tract by way of the blood stream. The cocci reach the urinary passages because they produce lesions in the glomeruli or capillary network of the kidney and thus break through into the tubular system. That bacteria are excreted by the intact kidney is no longer accepted as proved.

The relative frequency of coccal infection of the urinary passages of the adult male and of the adult female is practically the same. Hellström, in his series of cases, gave an almost equal quantity to represent coccal infections of the members of the two sexes; eighteen of the male and twenty-two of the female. In the same series the quantities he gave for bacillary infection were thirteen of the male and 120 of the female. Of children less than 15 years of age, six males and six females had staphylococcal infection, and five males and sixty-one females had bacillary infection. My figures representing bacillary infection of infants are that 86 per cent of the patients were girls and of older children, 75 per cent were girls. Inasmuch as bacillary infections are three to four times as common in the female as in the male, and inasmuch as coccal infections are about numerically equal in the two sexes, it is reasonable to suppose that the infections do not occur by the same route. This becomes even more likely when it is seen that, during the short neonatal period, when the colon bacillus is known frequently to invade the blood stream, bacillary infection of the urinary tract is just as common among boys as among girls.

This leaves as the route of infection, the direct ascent of the urethra and the passage of bacteria to the bladder by way of the lymphatic channels from the intestinal tract or the sex organs.

The argument is made that infection of the bladder cannot occur by way of the urethra, because it is impossible to infect the normal bladder merely by introducing bacteria through the urethra: however, the argument does not hold. It may be true if the bladder is normal, but when bacteria are introduced into a bladder which is not normal—for example, when there is an acute gastro-enteritis in infancy and no urine is excreted to wash out the urethra—the result may be entirely different. It is known that at such times bacilluria is frequently found and that it is about twice

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as common among female as among male infants. The facts that when there is diarrhea the genitalia are constantly bathed in fecal material and the urinary secretion is considerably reduced by the shunting of fluid through the gastro-intestinal canal, make it seem likely that the infection ascends through the urethra. If infection came by way of the blood stream or the lymphatic structures of the bowel, the incidence by sex should be the same. If, on the other hand, it is assumed, as has been done, that in the female vaginitis or cervicitis results first, and that one of these in turn gives rise to transparietal infection of the bladder, two assumptions are made instead of one, for neither of which is there any experimental evidence. As far as the lymphatic route into the bladder is concerned, no one ever has shown that the presence of bacteria in the tissues of the submucosa would cause an infection within the bladder unless rupture through into the vesical lumen took place. Cabot's and Crabtree's finding of Escherichia coli in the blood stream after instrumentation, before these organisms were found in the urine, is not absolute evidence that these organisms also were responsible for infection of the upper part of the urinary tract. At the same time, organisms may have brought about infection by the ascending route, for it is known from the results of Levy's studies of the blood and urine in puerperal infections with Escherichia coli, that the blood may contain many organisms per cc. and the urine may nevertheless be sterile. To be explained also are the frequent secondary bacillary infections after primary infection with one of the coccal forms. After a short time the bacillary infection may alone remain.

The entrance of bacilli as secondary invaders of the urinary passages by way of the blood stream is even more difficult to explain than their entrance as primary invaders. Experiments[9] carried out in 1923, in which infection of the urinary passages of rabbits was produced with staphylococci, did not show that Escherichia coli appeared in the urine with any regularity after its intravenous injection. After simultaneous injection of staphylococci and Escherichia coli, abscesses in the kidney and acute pyelitis were found at necropsy but only staphylococci were cultured from the urine. In like manner, Escherichia coli injected intravenously into rabbits suffering with staphylococcic pyelonephritis did not appear subsequently in the urine. It is known that infection does not persist in the bladder when infection introduced through the blood stream is eliminated from the upper urinary passages. Spontaneous bacilluria of the upper urinary passages is exceptional.

Thus there exists further evidence, by exclusion of the hematogenous route, that infection of the bladder with Escherichia coli is from below. Rarely is the normal bladder infected by catheterization even when the technique is improper. This is mirrored in the great difficulty to produce cystitis experimentally in the rabbit by introduction of massive doses of bacteria into the bladder. Yet it is known that bacilluria[6] limited to the bladder is the commonest disease of the urinary tract of the rabbit, probably representing its initial stage. Of thirty-eight cases of spontaneous infection, in thirty-four the condition was bacilluria and in only four, pyuria; therefore it seems likely that bacilluria is the primary stage of the infection. Lack of resistance of the mucosa or of the normal washing out of the bladder, allows the organisms to grow and produce bacilluria. Lowered resistance or increased virulence acts to set up inflammation in the wall of the bladder and to produce cystitis. For this reason it is fair to assume that the route of infection in bacilluria is by other than the blood stream, in all likelihood by way of the urethra. Thus, there should be no surprise that the immunity of the normal bladder to infections can change readily so as to allow bacteria to grow luxuriantly in its content. When one considers the many folds and crypts that are seen to exist in the female urethra,

according to the work of MacKenzie and Beck, and of Cabot and Shoemaker, it is surprising that residual infection does not more frequently occur when bacteria are carried in with a catheter.

INFECTION OF THE PELVIS OF THE KIDNEY

The second part of the ascent is from the bladder to the pelvis of the kidney. That this occurs readily whenever there is stasis and that infection travels up the column of stagnant urine is generally accepted. It is the case in which there is no stasis with which I am concerned. The two ascending routes of infection are, first, through the lumen of the ureter, and second, by way of the ureteral and peri-ureteral lymphatic channels. The loss of function of the ureteral valves, which may be owing to inflammation or may be of a functional nature, may lead to regurgitation of the infected content of the bladder. Such reflux has been shown to take place in animals as well as in human beings. The inflammatory exudate in the peri-ureteral lymphatic structures, both after vesical infection and after injection into the base of the bladder or into the uterine cervix, does not necessarily mean that infection of the renal pelvis will take place, but that it will take place has been assumed by some observers.

The human pathologic material does not give any help in the solution of this problem of infection of the renal pelvis, and it is necessary to rely almost entirely on experimental data and on study of the spontaneous disease in the animal. The material which should be available for study from patients with exstrophy of the bladder, who have died following transplantation of the ureters, is of very little use because of the extensive nature of the lesions and because obstruction is usually a complicating feature.

My material, obtained from experiments on ascending infection, dates back to the isolation of organisms of the colon group from a case of spontaneous pyelitis in the rabbit. The organisms, besides having specific localizing power in the kidney on intravenous injection, also had unusual powers of producing infection of the upper urinary tract when introduced into the bladder.[8] There were available for study thirteen positive experiments in which infection of the pelvis of the kidney was produced by the intracystic injections, by gravity, of from 5 to 8 cc. of a twenty-four hour broth culture. The animals lived from five to thirty days before they were killed. There was no growth on culture of the urine of each animal before the experiment was started. In two additional experiments there was no infection of the pelvis on either side, but cultures from the urine of one of the renal pelves were positive. In one of the thirteen experiments in which there was unilateral pyelitis, the culture from the kidney opposite to that of the pyelitis was positive for Escherichia coli. In these experiments all cultures taken from the heart blood at necropsy were sterile and involvement of the renal parenchyma was very slight.

In one of the foregoing series of experiments, the papillae gave evidence of the subepithelial infiltration which is common in the hematogenous type of infection, without the marked involvement of the parietal wall usually seen in ascending infections. Otherwise the parenchyma was negative. In two instances the inflammatory reaction was so severe that the substance of the kidney also was involved. In a fourth, and the only one of the series in which such phenomena were observed, a single group of abscesses was found in the cortex of both kidneys, thereby differing from the hematogenous infections, in which the abscesses were always diffusely scattered through the cortex.

These fifteen intracystic injections resulted in cystitis developing in all the animals; unilateral bacilluria of the renal pelvis in two animals; unilateral pyelitis together with unilateral bacilluria of the renal pelvis in one animal, and pyelitis in twelve animals. Of the last group (twelve animals) eight gave evidence of only simple infection of the pelvic lining, while four

gave evidence of involvement of the renal parenchyma. Of these four, in three the papillae were involved and in one there was a single group of cortical abscesses which could be traced up into the cortex from the papilla. When the conditions in the ureters were studied, it was found that of the fifteen positive experiments, in only three was peri-ureteral infiltration extending from the bladder to the renal pelvis discovered. In two of the three the process was bilateral, and in one, unilateral. (Fig. 1.) Thus, in twelve of the fifteen experiments in which bacteria were found in the renal pelvis after intracystic injection, the ureteral lymphatic structures gave no evidence of infection. The question arises as to whether the involvement of the ureteral lymphatic structures in the three cases necessarily had anything to do with the infection of the renal pelvis. As shown by the work of David and Mattill, an inflammatory exudate in the peri-ureteral lymphatic structures and in the submucosa of the pelvis is possible in the presence of a sterile urine. Therefore it seems likely that the infection, if it travels up the peri-ureteral lymphatic structures in ascending from the bladder to the pelvis, does so only in a small number of cases, and that there is a possibility that this involvement of the lymphatic structures, although present, may have nothing to do with establishment of the infection in the renal pelvis.

The work of David, as well as my own work, shows that, experimentally, ascending infections can occur without any evidence of peri-ureteral involvement of the lymphatic structures, and this forces me to make the same assumption as that made by David; namely, that the infection travels by way of the lumen of the ureter. The work of numerous observers who have found peri-ureteral pigment, bacteria or inflammatory material in the lymphatic structures has not proved that actual infection of the pelvis had occurred or, in some instances in which infection within the pelvis actually was present, that it had not occurred by way of the lumen of the ureter. Peri-ureteral inflammation of the lymphatic structures is not synonymous with infection of the pelvis of the kidney

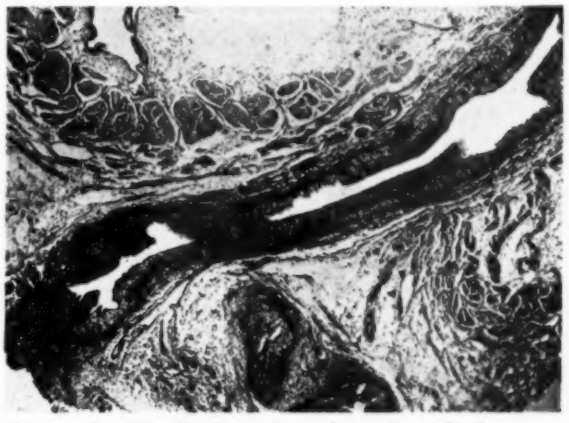

Fig. 1. Longitudinal section of cystic end of ureter. Intense ureteral and peri-ureteral inflammation.

and infection of the pelvis after intracystic injection is commonest without peri-ureteral inflammatory infiltration of the lymphatics.

Taking everything into consideration, injection of from 5 to 8 cc. of a twenty-four hour culture of colon bacilli is a rather crude means of determining the mode of travel of an infection from the bladder to the pelvis. The more surprising, then, are the many failures in producing even cystitis of any degree of severity or chronicity, except with exceptional organisms.

In my routine catheterization of rabbits and culturing of the urine, I was surprised to find that, in spite of the known difficulty in infecting the bladder, a large number of animals had bacilluria. Following up this lead, I was able to study, in animals, sixty-seven cases of infection of the urinary passages, thirty-four instances of bacilluria and thirty-three instances of pyuria. The instances of pyuria were culled from a large series of animals catheterized in a period of twenty years.[6] The fact that this group of sixty-seven cases consists of thirty-four instances of bacilluria and thirty-three of pyuria does not mean that it represents the true proportion of these entities. During the period that I was carefully studying both entities I found that of

thirty-eight cases of infection of the urinary passages, thirty-four were cases of bacilluria and only four were instances of infection evidenced by pus. That represents an incidence of pyuria of about 10 per cent. Later in my studies I did not keep track of the cases of bacilluria but studied only the cases of pyuria until I had a series of about an equal number of each. This group of sixty-seven animals, thirty-four of which had bacilluria and thirty-three, pyuria, represents a more complete series of the various stages of urinary infection than is anywhere available at present.

Spontaneous infection of the bladder by the ascending route has been covered in the previous section. Thus a start can be made here with infection present in the bladder in thirty-four cases of bacilluria and with seventeen cases of cystitis. In three of the thirty-four cases of bacilluria, and in three of the seventeen cases of cystitis (Table 1), the urine from the renal pelvis contained organisms but no pus cells. The pelvic bacilluria was bilateral in three cases and unilateral in three. As I interpret these findings, these six cases represent the first stage in the ascent of the infection from the bladder to the kidney, for there was bacterial contamination of the urine of the renal pelvis but no inflammatory reaction of the pelvic lining. This corresponds to the two cases of the experimental disease in which, after intracystic infection, there were organisms to be grown from the pelvis but no evidence of inflammation in the urine or the pelvic lining. Finally, there are sixteen cases of cystitis, with infection of the upper part of the urinary tract, of which eleven were cases of simple pyelitis in which the pelvis alone was the seat of infection. This represents the second stage in the ascent of the infection, in which there is an inflammatory reaction of the pelvic mucosa to the bacteria. In only six of these sixteen cases was there evidence of peri-ureteral inflammatory reaction. In addition, in the six cases of pelvic bacilluria previously mentioned, there was no evidence of peri-ureteral inflammation. The absence of peri-ureteral reaction in sixteen of twenty-two cases makes the lymphatic route of ascent much less likely than the one by the lumen of the ureter. This agrees closely with the presence of peri-ureteral infiltration in only three of the thirteen cases of experimentally produced infection of the renal pelvis.

Table 1
BACILLURIA OF THE RENAL PELVIS IN CASES OF CYSTITIS IN RABBITS

Rabbit	Urine					
	Bladder		Pelvis of Left Kidney		Pelvis of Right Kidney	
	Gram Negative Bacilli	Pus	Bacteria	Pus	Bacteria	Pus
1	Innumerable	+++	−	−	−	−
2	Innumerable	+++	−	−	−	−
3	Innumerable	+++	−	−	−	−
4	Innumerable	++++	−	−	−	−
5	Innumerable	++++	−	−	−	−
6	Innumerable	++++	−	−	−	−
7	Innumerable	++++	−	−	−	−
8	Innumerable	+++				
9	Innumerable	+++	+	−	+	−
10	Innumerable	+	−	−	−	−
11	Innumerable	++	−	−	−	−
12	Innumerable	+	+	−	−	−
13	Innumerable	+++	−	−	−	−
14	Innumerable	++++	−	−	−	−
15	Innumerable	++++	+	−	−	−
16	Innumerable	+++				
17	Innumerable	++++				

I want to emphasize this group of simple pyelitis in particular, because the occurrence of inflammation limited to the renal pelvis has been doubted by some observers, and because such inflammation resembles closely the lesions produced in the pelvis by injection into the transplanted ureters of dogs. Numerically more than twice as common as spontaneous pyelonephritis, a secondary involvement of the renal parenchyma, from the pelvis, probably took place in all but one of five cases of pyelonephritis.

THE ROUTE OF INFECTION OF THE PARENCHYMA FROM THE RENAL PELVIS

In this third part of the ascent of infection, use of pathologic studies on human material is of relatively little value. The renal parenchyma is usually so intensely and widely involved that the route of infection is completely obliterated. Only very occasionally are early lesions comparable to those experimentally produced in animals, seen in kidneys of man.

There are at least four ways by which infection can enter the renal parenchyma: (1) by ascent of the collecting tubules, producing local lesions in the papilla, medulla or cortex; (2) by extension along the perivascular lymph spaces of the large vessels which enter the substance of the kidney; (3) by the vascular route, in which either arterial or venous blood becomes infected directly from the adjacent infected pelvis, and (4) by direct extension through the wall of the pelvis into the renal parenchyma at any point where the parenchyma lies in direct contact with the pelvis. Such a point of direct contact, and one through which extension frequently occurs, is the place where the pelvic lining is reflected from the renal parenchyma.

In addition to the lymphatic and hematogenous routes, Hinman mentioned the pyelovenous, tubular, tubulovenous and tubulolymphatic routes, or the interstitial back-flow. He stated that when back pressure is present and infection of the blood stream has occurred, lesions may be produced when the organisms are excreted. In view of the presence of organisms in the renal tissue, it seems hardly necessary to assume a complete circuit of the infectious agent through the circulatory system and its return to the substance of the kidney. Hinman, as well as many others, stated that infection of the renal parenchyma from the pelvis is not likely to occur without some form of obstruction. The significance of this is evident when it is realized that to produce infection of the renal parenchyma, without back pressure, is difficult.

On the basis of the work done by Schmidt and Aschoff, MacCallum considered the first mode of infection the most likely one. Their experiments were with rabbits, the ureters of which were completely obstructed. They laid great emphasis on necrosis of the papillae, which, if one judges by their work as well as by my experimental work with sterile hydronephrosis,[10] is definitely anemic necrosis resulting from the cutting off of the blood supply. Necrosis of the papillary tubules can be observed even after twenty-four hours. As a result of experimental work as well as of study of post-mortem material, Kennedy rejected the hypothesis of ascent of the infection by way of the tubules and favored the perivascular route.

Müller, as a result of examination of human pathologic material only, came to the conclusion that infections enter the parenchyma of the kidney by way of the perivascular lymphatic structures, through extension between the tubules and finally through rupture of inflammatory products into the lumens of the tubules. Histologic studies in cases of the most acute infections, in one of which, for example, death occurred on the fifth day, have left me doubtful as to the course of the infection in children.

It seemed important here to supplement the human material with experiments on animals, and this in the absence as well as in the presence of stasis in the urinary passages. The series of experiments[7] consists of those carried out in the presence of completely obstructed urinary passages and of those made without obstruction. No experiments were carried out in the presence of partial obstruction.

The contrast between the two series of experiments is most striking and emphasizes again the important rôle that stasis plays in urinary infection. The lesions produced by Escherichia coli injected into the obstructed ureter were observed after eighteen, twenty-four, thirty, thirty-six, forty-eight and ninety-six hours.

As will be seen in Table II, five experiments were done with an eighteen-hour interval and six with a twenty-four hour interval between injection and termination of the experiment. These two sets of experiments, in which the intervals were short, were the most conclusive as well as the most interesting of all because they indicated the route of the infection in its earliest stages, before the various parts of the kidney had become involved. The lesions were essentially peritubular, perivascular and vascular and, in contra-distinction to the findings of Schmidt and Aschoff, changes were entirely absent in the medulla. The cortex, in two instances, was the site of abscesses after the interval of twenty-four hours. After eighteen hours the inflammatory process could be traced to the cortex, along the perivascular lymphatic channels. In Figure 2, which also shows the results of an experiment eighteen hours in duration, direct extension through the pelvic wall is seen at the point of reflection of the pelvic lining from the renal parenchyma. In this area thrombosis of a large vein also is observed. At this stage the papilla and the medulla of the kidney were entirely free from inflammatory reaction. Figure 3 shows a cortical abscess eighteen hours after injection of staphylococci into the obstructed ureter.

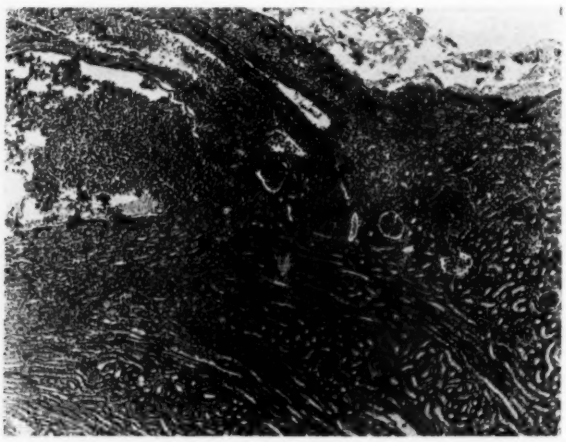

Fig. 2. Rupture of the pelvic lining, direct extension of the inflammation into the renal parenchyma and thrombosis of the vein.

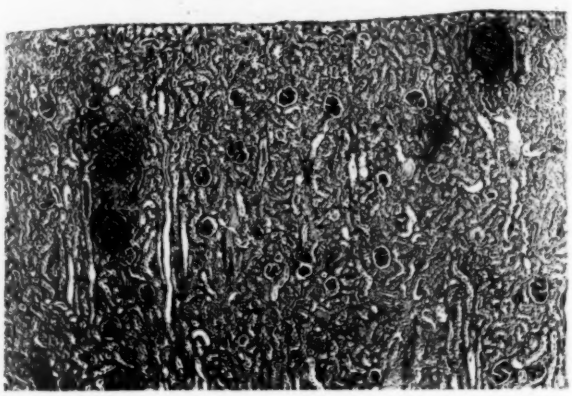

Fig. 3. Cortical abscesses eighteen hours after an injection into an obstructed ureter.

Table II

Parenchymal lesions following injections of bacillus coli into obstructed ureter

Time, Hours	Number of Experiments	Infection		Venous	Abscess	
		Peritubular	Perivascular	Thrombosis	Cortex	Medulla
18	5	3	3	2	0	0
24	6	4	5	3	2	0
30	5	3	3	5	1	0
36	4	2	3	3	1	1
48	4	4	4	4	4	4
96	1	1	1	1	1	1

(Helmholz. *Am. J. Dis. Child.* July, 1937.)

At the end of thirty hours it was observed that, in addition to the foregoing changes, the perivascular, peritubular and thrombotic lesions were the outstanding features, and there were still no changes in the medulla. The first abscess in the medulla was observed after thirty-six hours. After forty-eight hours, in the four experiments done (Table II), there were peritubular, perivascular and vascular lesions and abscesses in the medulla and the cortex. In other words, there was complete involvement of the parenchyma of the kidney within forty-eight hours when the ureter had been completely obstructed. Thus, only in experiments in which the interval was less than forty-eight hours was it possible to determine by what route the

various portions of the parenchyma had become infected.

It is thus evident that infection can enter the parenchyma by way of the perivascular lymphatic structures, by direct extension through the pelvic wall and by direct involvement of the vessels in the peripelvic tissue. The frequency and the extent of the thrombosis of the renal vessels make infarction an added factor in destruction of renal tissue. Focal lesions appeared first in the cortex as early as eighteen hours after injection and these lesions were followed by lesions in the medulla and the papillae. Whether infection ever spread by ascent of the collecting tubules must be left undecided but in this series of experiments no evidence of such ascent was found. The severe inflammatory reaction in the peripelvic tissues and the constant vascular lesions make the entrance of organisms into the blood stream easy, and it is likely that bacteremia is the rule rather than the exception in cases of this type of infection.

Fig. 4. A single group of cortical abscesses produced by ascending infection following an intracystic injection.

In a study of infection of the renal parenchyma from the pelvis, when there was no ureteral obstruction, a different picture was found. The lesions usually were few but on occasion were so extensive that the route of infection was practically obliterated. The usual picture was that of acute pyelitis, more marked on the parietal surface, with the renal parenchyma offering a definite barrier to infection. In only one of the fifteen experiments in which my co-worker and I[8] attempted to produce pyelitis by injection of colon bacilli into the bladder were we able to produce an extensive renal lesion and this consisted of a single group of abscesses in each kidney. (Fig. 4.) At a later date, by injection into the bladder of virulent strains of Escherichia coli, together with foreign bodies, we were able to produce pyelitis in four of eight rabbits; but in only two of these were we able to produce any changes in the parenchyma of the kidney. As in the experiments in the presence of obstruction, the lesions were in the nature of perivascular infiltrations along the large vessels, venous thrombi and peritubular infiltrations extending out from the thrombotic portions. (Fig. 5.) In spite of intensely inflammatory lesions in the peripelvic tissues, amounting in some portions to actual abscesses and multiple mural thrombi of the veins, no definite abscesses were seen in the renal parenchyma. The papillae and the medulla were free from inflammation. Along the large vessels were inflammatory lesions and the bacteria extended into the cortex of the kidney. In a number of regions of multiple venous thrombosis the inter-

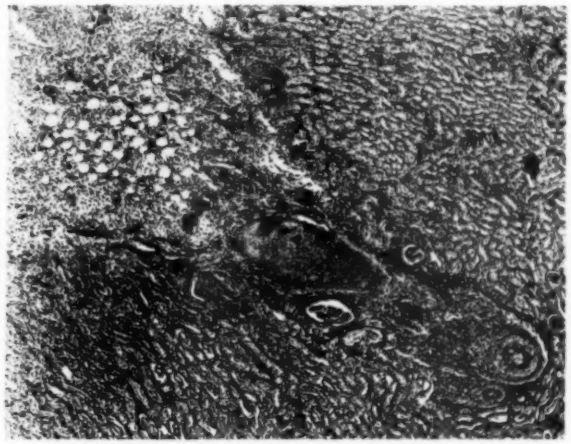

Fig. 5. Multiple thrombi and intertubular infiltration into the kidney after an intracystic injection.

tubular inflammatory reactions were intense.

The series of experiments in which

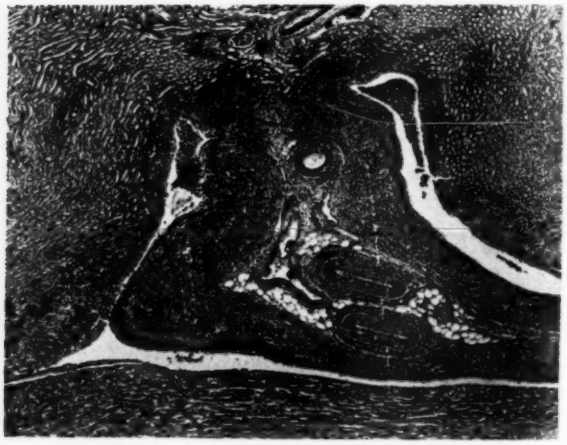

Fig. 6. Pyelitis, especially inflammation of the visceral layer, following an intra-ureteral injection.

spontaneous pyelitis developed in rabbits furnished only one example of extensive involvement of the renal parenchyma. The lesion in these experiments, as in the experiment in which an abscess of the cortex was produced by cystic injection, was a single large group of abscesses. The nature of the path of the infection from pelvis to parenchyma could not be made out but the similarity of the lesions is interesting especially as there was a similar one in the animals that had received ureteral injections.

The uncertainty of producing pyelitis by intracystic injection interrupted our experiments for a number of years. Recently, however, through the coöperation of Mann and his staff, a series of rabbits and of dogs in which the bladder had been transplanted into the anterior abdominal wall has been made available. These animals furnished ideal material for producing pyelitis in the unobstructed urinary tract. Ureteral urine could be obtained directly from each kidney and a bacterial suspension could be injected into the pelves of the kidneys.

In the first experiments, only one ureter received an injection, and the other kidney was kept as a control. After it was seen that a number of control kidneys were normal, each animal was used for two experiments; the material was injected into one kidney on a certain day and into the

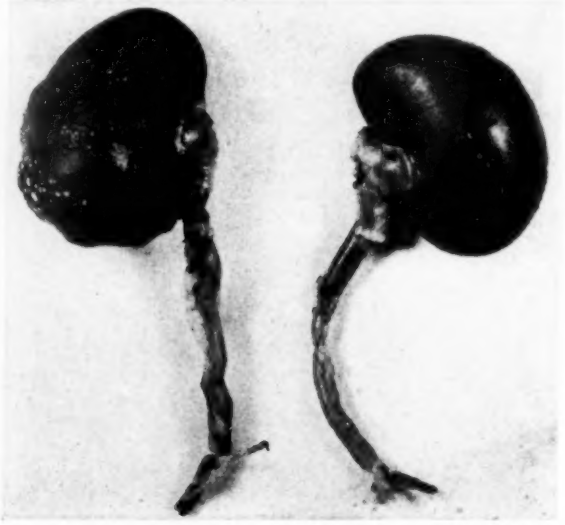

Fig. 7. Multiple abscesses in the cortex of the kidney of a rabbit, complicating hydronephrosis after an intra-ureteral injection. (Tables II and III and Figures 2 to 7 also appear in *Am. J. Dis. Child.*, July, 1937.)

other a few days later. In this manner, eighteen experiments were carried out. In Table III the results of these experiments are recorded.

The striking feature was the absence of parenchymal lesions in the kidneys. In only two animals were there definite lesions at a distance from the pelvis. In one animal, a dog that had to be killed because it was extremely ill, multiple abscesses were observed in the medulla and in the papilla of the kidney five days after the first injection and two days after the second injection, but these apparently were not related to the mild inflammation of the pelvis of the kidney. In the other animal, one kidney exhibited lesions which were limited to a single large group of abscesses. This group of abscesses closely resembled the single cortical abscess produced by intracystic injection as well as the single group of abscesses observed in the rabbit which had spontaneous pyelitis.

In the other sixteen of the eighteen experiments, the lesions, although extremely severe and acute, were limited to

the immediate vicinity of the pelvis. In the epithelium there were many cysts filled with pus cells but no vascular thrombi were seen. The parietal side of the pelvis was edematous and densely infiltrated with many polymorphonuclear leukocytes and young connective tissue cells. (Fig. 6.) The absence of inflammatory reaction in the opposite kidney, used as control, is seen. In the visceral side of the pelvis there was much less infiltration, and often this process was entirely absent. In only one instance was there considerable intertubular infiltration and hemorrhage.

Table III
Infection of the Kidney in Dogs with Exstrophy Following Ureteral Injection

Experiments		Infection of Kidney			
			Parenchymal lesion		
Duration, Days	Number	Pyelitis	Peripelvic	Papilla	Cortex
2	2	2	2	1*	1*
3	1	1	1	0	0
4	1	1	1	0	0
5	6	6	6	1†	1†
6	3	3	3	0	0
20	1	1	1	0	0
39–54	4	4	2	0	0

* Extremely sick dog, with mild pyelitis.

† Pus cells in the urine before injection; one large group of lesions.

(Helmholz. *Am. J. Dis. Child.* July, 1937.)

Of seven rabbits used in experiments similar to those just described, lesions were found in the renal parenchyma of only one, and in this animal, owing to a faulty operative procedure, definite hydronephrosis of both kidneys had been produced. The kidney on the side of the injection was extensively studded with cortical abscesses and in the control kidney there was similar hydronephrosis without the abscesses. (Fig. 7.) In the lining of the renal pelves of the other animals there was only inflammatory reaction.

This group of experiments shows characteristically that, even with the intense pyelitis produced by direct injection of bacteria into the pelvis of the kidney, a barrier to the spread of infection into the renal substance seems to exist. These experiments bring out most clearly that in the unobstructed urinary tract such an entity as pyelitis can exist, that the kidney has a protective mechanism by which the spread of infection is kept from the kidney proper, and that this barrier seemingly remains intact as long as there is no obstruction to the outflow of urine. It is broken down in less than twenty-four hours when there is complete obstruction. A series of experiments with more highly virulent organisms might give a different result, although one of the organisms used was isolated from the urine of a dog suffering from fatal pyelitis.

SUMMARY AND CONCLUSIONS

Coccal infection of the male and the female occurs with equal frequency. Bacillary infection of the female occurs three to four times as frequently as bacillary infection of the male. Coccal infection occurs by way of the blood stream, while bacillary infection occurs by routes other than the blood stream. The inability to infect the bladder of man has its counterpart in the inability to produce infection of the bladder of the rabbit by injection of massive doses of bacteria, and yet bacilluria limited to the bladder is definitely the most common spontaneous disease of the urinary tract of the rabbit and it may be the initial lesion of the human being. The greater frequency of bacillary infection of the female would lead to the belief that the infection occurs by way of the urethra, and although lymphogeneous infection must be considered a possibility, there is no definite proof of its occurrence. It is impossible from human material at the present time, to give any definite answer to the question. However, it is evident that two factors are necessary for infection of the bladder; namely, lowered resistance of the mucosa and bacterial invasion.

The experimental production of infection of the renal pelvis from the bladder has been accomplished by intracystic injection of bacteria into the bladder. The histologic picture of pelvic inflammation differs from that seen when the pelvis is infected by way of the blood stream. Histologic studies of the ureter have shown that in only three of thirteen cases was there any evidence of peri-ureteral inflammation. Therefore, unless it is assumed that infection can spread by way of the peri-ureteral lymphatic structures, without leaving a trace behind, it must be assumed that in the other ten cases the infection spread by way of the lumen of the ureter. The same conclusion must be drawn concerning spontaneous pyelitis of rabbits in which, in only six of the sixteen cases, evidence of peri-ureteral infiltration was found. Taking this in conjunction with the work of David, which shows that peri-ureteral inflammation does not of necessity mean infection of the pelvis, causes me to assume, until more definite information is available, that the usual spread of infection from the bladder to the pelvis is by way of the lumen of the ureter.

With stasis, the parenchyma of the kidney rapidly becomes infected from the pelvis by way of the perivascular lymphatic structures and by direct passage of the organisms through the pelvic lining over the parenchyma. Thrombosis forms an important feature of the renal changes. Without stasis, infection of the pelvis tends to remain local and only exceptionally does infection spread to the parenchyma by the same channels.

The striking difference between the two series of experiments shows that stasis is the all important factor in producing ascent of infection from the pelvis to the renal parenchyma.

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THE TREATMENT OF URINARY INFECTIONS

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THE foundation for the modern treatment of urinary infection was laid twenty years ago by the publication of two articles, one by Schohl and Janney[11] on "The Growth of Bacillus-coli in Urine at Varying Hydrogen Ion Concentrations" and the other by Gross[5] on the "Use of Neo-arsphenamine in Coccus Pyelonephritis." Treatment by means of acidification did not follow this article for many years, perhaps because of technical difficulties in determining the hydrogen ion concentration. It was not until 1932 that Clark[2] and Helmholz,[6] working independently, demonstrated that acidification and ketosis produced a bactericidal urine. Since then deliberate controlled acidification has been a valuable adjunct in the treatment of bacillary infections. Neo-arsphenamine has been used sporadically by many physicians in coccus infections and by some with good success.

Diagnosis. It is evident that before either of these methods of treatment can be employed, a diagnosis of the type of infection must be made. Many physicians have the idea that in order to do this special training in bacteriology is required. This is certainly not the case, as a stain of the urine sediment is all that is necessary to make the diagnosis in a high percentage of cases. Table I shows the comparison between stain and culture in making the diagnosis of urinary infection. It is seen that the stain is far superior to the culture (on blood agar) in making the diagnosis of coccal infections and practically as good as the culture (on Endos media) in making the diagnosis of bacillary infections. Seidman[12] discusses reasons for these differences, and points out how carefully certain organisms must be handled in order to have the culture succeed in identifying the bacteria. One can rarely make a diagnosis of urinary infection when the bacteria cannot be found in the centrifuged specimen. The urine in the female must be collected by catheterization; a satisfactory specimen for examination in the male is obtained by examination of the second portion of the voided urine. Examination should be made promptly after the urine is obtained. The gross appearance is noted and the pH checked. A centrifuged specimen is then examined for the amount of pus cells and red blood cells. Crystals should be noted. A gram stain on the sediment is next done and the number and variety of bacteria noted. The overwhelming majority of bacteria found in urinary tract infection are either gram-positive cocci shown in Figure 1 or gram-negative bacilli shown in Figure 2.

Another laboratory examination, necessary antecedent to the proper treatment of patients with urinary tract infection, is the determination of the hydrogen ion concentration or the pH. Many physicians believe this to be a difficult procedure, but modern colorimetric methods have made it very simple. Either a few drops of dye may be added to the urine and the color compared with a standard chart or dye impregnated paper is saturated with urine and the color again compared with a standard.

Coccus Infections Treatment. The relative incidence of coccus and bacillary infections is shown in Table II. It is seen that though the bacilli cause the great majority of urinary tract infections, enough infections due to cocci occur to make their treatment worth considering. The etiology of urinary tract infections will not be discussed here but certainly foci of infection play some part, and especially is this true in the coccal group. We have seen many patients in whom treatment has failed until foci were treated. The prostate and cervix must be remembered as such foci.

In our hands neoarsphenamine has been the most successful drug for eradicating coccal infections. Its mode of action is still in dispute, but Pace[9] believes that sufficient arsenic is eliminated in the urine to produce a bactericidal effect. Clinically this is supported by the fact that acidification seems to increase the efficiency of the drug, but it is refuted by evidence that infections limited to the bladder do not respond as well as do those in which the kidneys are also involved. The most efficient and best tolerated dosage scheme is to give .2 gm. followed in five to seven days by .3 gm. If no improvement results after these two injections, it is rare for a third dose to produce good results. If, however, there is no contraindication or arsenic reaction and if the patient has no demonstrable foci a third injection of .4 gm. may be given. We do not believe in further injections but turn to other methods of treatment. Acidification and urotropin, the azo dyes and hexylresorcinal are sometimes of value. Vaccine therapy, the vaccines being prepared from urine, throat, and prostatic or cervical cultures may succeed when other methods fail. The use of mandelic acid and sulfanilamide will be discussed later.

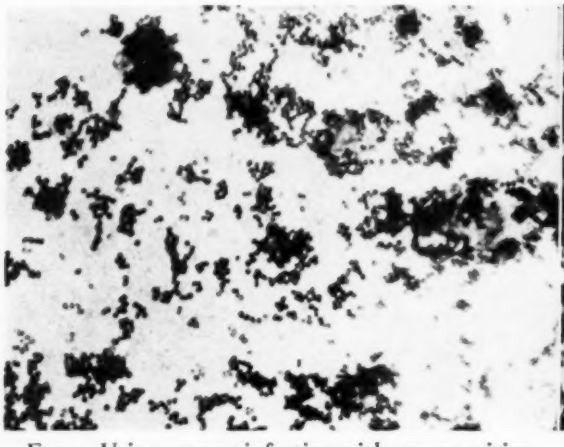


Fig. 1. Urinary tract infection with gram positive Cocci.

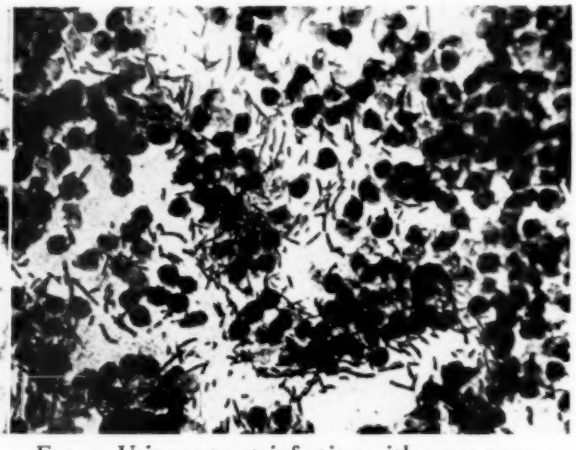


Fig. 2. Urinary tract infection with gram negative Bacilli.

Table 1

The relative efficiency of the gram's stain of the urine sediment and the culture of the urine in making a diagnosis of urinary infection

	Bacillary Infections		Coccal Infections	
	Number	Per Cent	Number	Per Cent
Stains and cultures agree	519	79	158	56.4
Negative stain and positive culture	102	15.6	30	10.4
Positive stain and negative culture	32	5.4	92	33.2
Total	653	100	280	100

The above plan of treatment does not hold for infections with the Streptococcus fecalis as this organism responds poorly to neoarsphenamine. As is seen from Table II, this is a rather common organism (12 per cent). Usually it can be differentiated from the other cocci by microscopic examination, and Figure 3 shows a typical smear of a urinary infection with Streptococcus fecalis. This organism is very resistant to sulfanilamide treatment but responds well to acidification and ketosis or to mandelic acid.

Bacillary Infections. Urinary tract infections due to gram-negative bacilli respond well to acidification and mandelic acid and somewhat better to alkalization and sulfanilamide.

Since we believe that in the present state of our knowledge the former is a less objectionable method of treatment, it

should as a rule be used. While the ketogenic diet was originally conceived as a method of acidification of the urine, it was soon evident that its effect was more potent than could be attributed to acidification alone. Fuller[4] soon found the explanation for this in the discovery that one of the ketone bodies, betahydroxybutyric acid, had bactericidal properties. This led Rosenheim[10] to an intensive investigation of the organic acids in the hope that one of them could be given by mouth and excreted unchanged in the urine. Mandelic acid was found to meet the requirements most fully and in addition was non-toxic enough so that adequate dosage could be given to produce a bactericidal urine. Experimentally, Osterberg and Helmholz[7] determined these levels and their results are shown in Table III. It will be noted that Pseudomonas and Aerobacter aerogenes are more resistant to the action of mandelic acid. In practice we given 12 gm. of ammonium mandelate daily in divided doses. This can be given in liquid form, or for those who object to the taste, the drug is available in tablets and capsules. Sodium mandelate seems to cause less gastric disturbances than do the ammonium salts but when this is used, additional acidification by means of ammonium nitrate or chloride is usually necessary.

Table II
URINE CULTURE FINDINGS. (FROM CABOT, MODERN UROLOGY, VOL. II)

	Number	Per Cent
Escherichia coli	490	55.9
Aerobacter aerogenes	91	10.4
Proteus ammoniae	48	5.5
Proteus (species?)	9	1.0
Pseudomonas aeruginosa	32	3.6
Pseudomonas (species?)	11	1.2
Salmonella (species?)	12	1.4
Alcaligenes (species?)	10	1.1
Eberthella typhosa	2	0.2
Shigella (species?)	6	0.7
Gram-negative bacillus (unidentified)	23	2.6
Streptococcus fecalis	105	12.0
Streptococcus (green producing)	10	1.1
Streptococcus (slight hemolysis)	33	3.8
Staphylococcus aureus	10	1.1
Micrococcus (species?)	132	15.0
Diphtheroids	4	0.4
Neisseria gonorrhoeae	1	0.1
Total number	877	

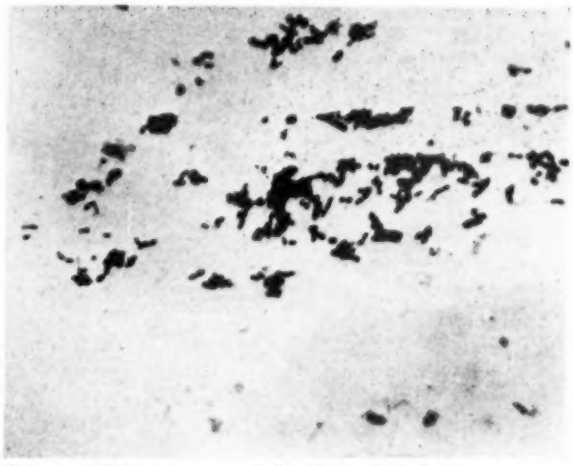


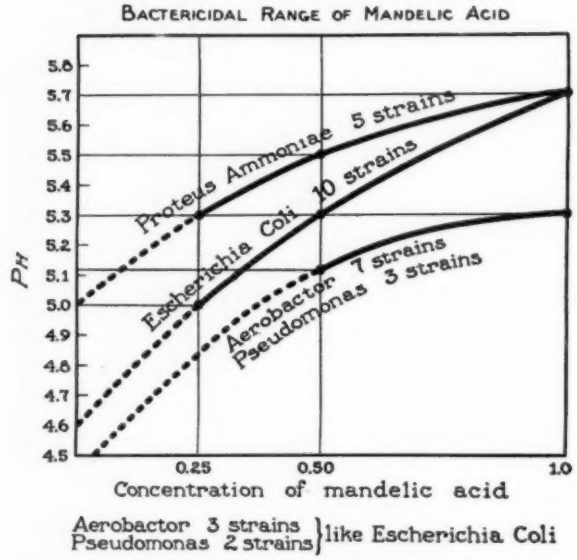
Fig. 3. Urinary tract infection with Streptococcus fecalis. Typically this organism occurs as oval cocci joined together by the end with a refractile streak down the center. The former feature is shown in the photomicrograph. The refractile streak is not shown. Sometimes cocci which do not show these characteristics will prove on culture to be Streptococcus fecalis. If these characteristics are not shown, the organism cannot be differentiated by the stain.

As is seen from Table III, the most important factor in the production of bactericidal urine is adequate control of the acidity. This should be checked frequently during the course of treatment and be kept, if possible, below 5.2. Usually such an acidity can be obtained by the use of the ammonium salt, but should this not occur additional acidification by means of ammonium nitrate, or chloride, dilute hydrochloric acid or an acid-ash diet is necessary. It is of the utmost importance that the patient take no alkalies, of which soda and saline laxatives are the most common. Patients in whom acidification is obtained with difficulty should abstain from toothpaste. Even with all these precautions, patients will be encountered in whom proper acidification is impossible.

In addition to proper acidification, adequate concentration of the drug is also necessary. Since there is no simple test for

the concentration of mandelic acid in the urine, the test being that for organic acids, the majority of our patients are treated with this as an unknown factor. If the fluids are limited so that the urinary output is around 1000 c.c. daily, adequate concentration will develop except when there is poor renal function.*

TABLE III*
THE BACTERICIDAL RANGE OF MANDELIC ACID



Aerobactor 3 strains, Pseudomonas 2 strains } like Escherichia Coli

* From H. F. Helmholz and A. E. Osterberg, Rate of excretion and bactericidal power of sulfanilamide in the urine. *Proc. Staff Meetings of the Mayo Clinic*, 12: 377–381 (June 16) 1937.

Excretory urography, since it tests the function of each kidney separately, provides a most satisfactory method of determining renal function when using excretory antiseptics. If the kidney visualizes well in five minutes after injection of the drug, it has adequate function. It must always be remembered that in unilateral kidney disease the bladder urine may be bactericidal while urine from the diseased kidney is not.

We do not believe that mandelic acid therapy should be continued for more than two weeks. At the end of that time, if improvement has not occurred, the drug is discontinued for a week or ten days. A second course may prove more beneficial than the first.

Mandelic acid used as has been described will prove successful in more than 90 per cent of uncomplicated bacillary infections, and is about 50 per cent efficacious in bacillary infections complicated by prostatitis, mild urinary obstruction, or chronic pyelonephritis without great renal damage. In our experience the Aerobacter aerogenes responds practically as well as the other bacilli. Failure will be the rule in the presence of lithiasis, foreign body, severe urinary obstruction or chronic pyelonephritis with marked renal destruction.[3]

Coccal infections, with the exception of Streptococcus fecalis, respond but poorly. Good results, however, are often obtained when the infection is confined to the lower urinary tract.

In resumé then, the coccal infections of hematogenous origin seem to respond to neoarsphenamine, while those of ascending origin respond to mandelic acid. Since the coccal infections of childhood are almost invariably of the latter type, drugs other than mandelic acid have little place.

Mandelic acid has little if any effect on normal kidney function. In fact, experimental animals show more liver than kidney damage. There is no doubt, however, that the drug is a renal irritant, as it is common to find red blood cells or casts in the urine of patients under treatment. Gross hematuria is rare.

Patients with reduced renal function must be treated with the greatest care, as treatment by acidification runs considerable risk of producing acidosis. Such patients must be carefully watched and their blood chemistry frequently checked. Acidification by means of ammonium nitrate is safer for this group than with ammonium chloride.

Gastro-intestinal upsets are infrequent, as are general toxic disturbances such as tinnitus, vertigo, palpitation, and dermatitis. Such reactions call for reduction of dosage or discontinuance of the drug. Very

* Mandelic acid is of great value in the treatment of acute urinary infections. When so used, the fluids must not be limited, especially if there is fever.

rarely these reactions may prove very severe.

Sulfanilamide. The most recent drug used in urinary tract infections has a longer history than either of the previous methods of treatment, as the original prototype of sulfanilamide was prepared as an azo dye in 1909. Its use in urinary infections, however, has developed within the past year, when many physicians, encouraged by the good results obtained in sepsis elsewhere in the body were led to try it in urinary tract infections. Strangely enough it has proved of greater value in bacillary than in coccal infections. Experience with this drug suggests that it is a more potent antiseptic than mandelic acid. This drug is also active in an alkaline urine and will develop a bactericidal urine in the presence of marked renal insufficiency. It is eliminated in good concentration in the urine but in poor concentration in the prostatic secretion.[1] In spite of this, a very salutory effect or prostatitis is noted. Urinary tract infection associated with prostatitis is eradicated as easily by sulfanilamide as other methods of treatment clear up uncomplicated urinary tract infection. The drug will not sterilize the urine immediately following prostatic resection, but has been the most successful drug we have to clear the urine before prostatic surgery. The proteus bacillus responds as well as the other bacilli. Failure usually results in the presence of lithiasis or chronic pyelonephritis with renal destruction. Bacillary infections respond better than coccal infections, and especially does this hold for Streptococcus fecalis where good results will practically never be obtained. This has been a most successful method of treatment of gonorrhea of both men and women.

From the discussion above, sulfanilamide would seem to be the drug of choice in the treatment of all bacillary infections, and were it not for the frequent reactions which follow its use such would be the case. While it is unnecessary to produce even the slightest reaction to obtain a favorable result, it is almost invariable that some malaise, dizziness, and headache develop. If these are relieved by rest, it is not necessary to reduce the dose. The occurrence of any other reaction calls for reduction in dosage or discontinuance of the drug. The number and variety of reactions that can be produced by sulfanilamide is legion. We consider cyanosis, hemoglobinuria, anemia or leukopenia, fever, dermatitis, and jaundice to be serious and call for cessation of treatment. Dermatitis and anemia or leukopenia are probably good reasons for permanently discontinuing the drug.

The mode of action of this drug is as yet not well understood. Experimentally, a urine to which sulfanilamide has been added will not have the bactericidal power of a urine produced in the body containing the same sulfanilamide concentration.[8] Experimentally the drug seems to work better in a urine of pH of about 7.5, and even though this cannot be supported clinically, there is certainly no objection to giving alkalies during treatment. Magnesium sulfate should not be given.

There is as yet no accepted dosage scheme for this drug. We start with a daily dose of 60 to 80 grains in four doses. After one to two days the dose is reduced and after another two days the patient is placed on a maintenance dose which is usually 40 grains daily. This is continued for not longer than ten days. Patients with gonorrhea, once clinical cure is obtained, are placed on a 20 grain daily dose for two weeks. Using this dosage scheme we have not seen the frequent recurrence in Neisserian infections that others have reported. In spite of frequent re-examinations after discontinuing the drug, all our patients have remained well. Our results using this dosage scheme have been so superior to those obtained by small doses that we plan to continue its use. Fifteen per cent of patients cannot tolerate this dosage. About 5 per cent will either respond to small doses or can gradually work up to a larger

dose. The remainder are intolerant to this method of treatment.

SUMMARY

Proper treatment of urinary tract infections depends upon a rough identification of the bacteria in the urine by means of a gram-stain of the centrifuged sediment.

Neoarsphenamine is the most efficient drug in the treatment of coccal infections, especially if these be of the hematogenous origin.

Acidification and mandelic acid is a most successful treatment for ordinary bacillary infections and coccal infections of the ascending type, especially Streptococcus fecalis.

Sulfanilamide should be used when mandelic acid fails and especially when acidification of the urine is impossible, such as occurs in Proteus infections, or when there is renal insufficiency. It is also the treatment of choice where urinary infection is complicated by marked prostatitis, and in Neisserian infections.

Any method of treatment is attended by a high percentage of failure in the presence of lithiasis, chronic pyelonephritis with marked renal destruction, or immediately following prostatic surgery.

Attention to foci of infection is important not only in treatment but also in the prevention of recurrences. The cervix and prostate must not be forgotten in the routine focal check.

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DIAGNOSIS AND TREATMENT OF PERINEPHRITIC ABSCESS: RENAL FIXATION, A NEW ROENTGENOGRAPHIC DIAGNOSTIC SIGN

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PERINEPHRITIC abscess is of great interest to all studying kidney diseases because there is still difficulty in its diagnosis resulting from meager clinical signs, obscure symptoms and lack of urinary disturbances. Inasmuch as we have discovered a new roentgenographic diagnostic sign we have lessened this difficulty. Although the majority of cases are now recognized by certain well-known signs obtained by making the present day urological investigations, there still remains a group of cases in which the diagnosis is difficult and in which our sign is most significant. This study is based on twenty-seven cases of perinephritic abscess which were corroborated by operation and in which a complete urological examination was made. The high mortality accompanying this disease should act as a stimulus in its early diagnosis, at which time drainage is most likely to be followed by relief of symptoms. In order intelligently to treat perinephritic abscess, one must be familiar with different types of abscesses resulting from distinctly different etiological factors. Therefore, in discussing its diagnosis and treatment, it is well to review the classification of suppurative perinephritis.

I. Primary Metastatic Type. (Independent of kidney lesions or those of neighboring thoracic and abdominal organs).

a. Hematogenous: secondary to foci elsewhere in the body—skin lesions such as boils, furuncles, carbuncles, impetigo, eczema, paronychia, infected vaccinated areas, osteomyelitis, tonsilitis, prostatitis, etc.

b. Toxic or hematogenous: secondary to generalized infections such as smallpox, scarlet fever, typhoid fever, influenza, puerperal fever, anthrax, gonorrhea, etc.

c. Traumatic: caused by lowered resistance of perirenal tissues resulting from contusion, infection of small and large hematomata, wounds, etc.

II. Perinephric Abscess. Secondary to the following kidney lesions:

a. Cortical abscess formation, carbuncle, pyelonephritis, pyonephrosis, tuberculosis, lithiasis, infected polycystic disease, spontaneous and traumatic rupture, etc.

b. Post-operative: abscess formation after nephrectomy: secondary to silk sutures, to leaving portions of infected kidney behind, to tuberculous involvement of the perirenal tissues and to insufficient drainage after kidney operations such as pyelotomy, nephropexy, plastic repair, etc.

III. Paranephritic Abscess. Secondary to following extraneous lesions:

a. Suprarenal diseases such as Addison's disease, infections of adrenal gland, etc.

b. Intestinal lesions: appendicitis, infections of the duodenum, intestines and colon.

c. Affections of the abdominal and pelvic organs: spleen, pancreas, prostate, gallbladder, uterus in which parturition and abortion play a rôle, etc.

d. Infections of the skeletal and muscular structures making up the renal fossa: tuberculosis of the spine, myositis of psoas muscle, etc.

e. Thoracic lesions: suppurative pleurisy, lung abscess, suppurative mediastinitis, etc.

f. Unusual conditions: secondary to foreign bodies such as bullets, etc.

ETIOLOGY

The etiology of the primary metastatic type caused by septic emboli forming foci of infection transmitted by the blood stream and secondary to infections of the skin, respiratory tract, prostate gland, etc., has been the subject of considerable speculation. Since Jordan correlated the relation of skin infections to perinephritic abscess, in 1905, this type of infection has been intensely studied. It was found that many abscesses were secondary to cortical abscess of the kidney, single and multiple and to carbuncle; in some instances the cortical abscess is so small that it is easily overlooked at the time of operation. Many writers feel that the majority of the metastatic type of perinephritic abscess are secondary to cortical abscess formation in the cortex of the kidney, be it by direct invasion of the perirenal fat by necrosis, by the blood stream, or by way of the lymphatics. Supporting this theory, Guiteras (1906), Murphy (1914), Braasch (1915), Hunt (1924), Lott (1926), Birdsall (1932) and others stated that the greater majority resulted from direct cortical infection of the kidney. On the other hand, Rehn (1911) and Doberauer (1915) pointed out the fact that hematogenous infection of the perirenal fat may occur independently of the kidney, the selective organisms forming infective emboli in the network of end arteries made up by the capsular branches supplying the perirenal fat, including the renal, suprarenal, superior mesenteric, inferior mesenteric, spermatic, aortic, ovarian, lumbar, colic, etc. Vermooten (1933) reported autopsy findings in a case of bilateral perinephritic abscess in which a minute histo-pathological study of both kidneys failed to reveal any sign of infection. We have intervened on a goodly number of patients presenting the metastatic hematogenous type of perinephritic abscess in whom careful examination of the cortex of the kidney at the time of operation failed to reveal the slightest abscess. Although a considerable number of the metastatic type of perinephritic abscess are secondary to cortical abscess of the kidney, there is unquestionably a number of cases in which infection takes place primarily in the fat, independent of the kidney and we acknowledge that this type of disease is a definite clinical entity having no relation to infection of the kidney cortex.

The secondary type of perinephritic abscess resulting in abscess formation of the perinephrium, secondary to kidney disease such as pyonephrosis, tuberculosis, lithiasis, spontaneous and traumatic rupture, infected polycystic disease has been recognized ever since the time of Hippocrates. In these a complete urological examination will usually reveal the primary inflammatory lesion in the kidney which has extended to the perirenal fat resulting in abscess formation. Numerous observations of this phenomenon have been reported and to mention a few I call your attention to A. R. Stevens (1926) who reported perinephritic abscess secondary to ruptured diverticulum of the upper ureter; Gruenfeld and Sigoloff (1930) who reported abscesses associated with gall-bladder and duodenal disease; Lavenant (1928) and Gayet (1935) abscesses resulting from tuberculosis; to Vecki (1932) and Twinem (1936) abscesses due to infected polycystic kidney disease, and to the author (1932) abscesses secondary to spontaneous rupture of the kidney, etc.

Perinephritic abscess secondary to extraneous infection of neighboring structures and organs requires careful study. Of interest is the post-operative perinephritic abscess following nephrectomy, pyelotomy, plastic repair of the pelvis, nephropexy and other conservative surgical interventions on the kidney, due to insufficient drainage of the renal fossa. Those resulting from infected hematoma occasioned by trauma have elicited interest from their legal compensation aspect. Giordano reported an interesting case in which an abrasion of the skin of a workman's leg obtained while at work became infected and resulted in the hematogenous type of perinephritic abscess

which assumed compensatory responsibility on the part of the employer.

DIAGNOSIS

The first group consisting of the primary metastatic type of suppurative perinephritis offers a great problem for diagnosis. The second group, the secondary type of perinephric abscess, always accompanies a well developed kidney lesion, viz: tuberculosis, lithiasis, calculous pyelonephrosis, spontaneous and traumatic rupture of the kidney, etc., and a careful urological study in these cases usually points the way towards the diagnosis of abscess formation of the perirenal tissues. The third group of paranephritic abscess is quite obscure, being secondary to extraneous lesions in surrounding abdominal, pelvic, thoracic and perirenal organs and in the skeletal muscular structures making up the renal fossa. Diagnosis of this type of abscess requires cooperation of the urologist with the surgeon and the internist. (Table 1.)

Table 1

CASES OF SUPPURATIVE PERINEPHRITIS DIAGNOSED BY COMPLETE UROLOGICAL EXAMINATION

1. Primary metastatic hematogenous type of perinephritic abscess	9
2. Secondary perinephric abscess	14
a. Hematogenous abscess of renal cortex, 3.	
b. Kidney lesions, calculous pyonephrosis, 3.	
Tuberculosis, 1.	
Lithiasis, 5.	
Rupture, 1.	
c. Postoperative, 1.	
3. Secondary paranephritic abscess	4
a. Pott's disease, 3.	
b. Gangrenous appendicitis, 1.	
Total	27

Note: 29 other cases eliminated from series because of incomplete data.

Clinical Signs and Symptoms: A careful history is most important. The development of fever usually ushered in by a chill, accompanied by pain and tenderness in the loin or upper abdomen, leucocytosis, signs of psoas spasm, evidenced by changes in posture, flexion of the thigh, anorexia, nausea and vomiting, loss of weight, etc. occurring in a few days to a number of weeks after skin infections, tonsilitis, prostatitis, etc., in which there is a paucity of urine findings, should make one suspicious of the metastatic type of perinephritic abscess. This type of disease has been confused with neurasthenia, rheumatism, hip joint disease, tuberculosis, malaria, typhoid and tropical fever, pyelitis, etc. All regional structures should be considered in its differential diagnosis. In the past, many perinephritic abscesses were confused with tuberculous hip disease and Pott's disease, especially in children (Elmer). More recently, numerous are the urologists who, in their zeal to detect early perinephritic abscess, have been misguided by diseases of the neighboring structures and organs which gave signs and symptoms suggestive of perinephritic abscess. The author operated on a child, 11 years of age, presenting signs and symptoms of perinephritic abscess in whom early Pott's disease was encountered. Huc reported an interesting case of infected renal cancer simulating perinephritic abscess. Alcock emphasizes the number of retrocecal abscesses that are confused with perinephritic abscess. Kessler, Bennetts and Bacon pointed out the frequency of lesions of adjacent bones simulating this condition. Rusché and Bacon reported ten cases of interesting extraneous lesions all of which were operated for perinephritic abscess.

Perinephritic abscess usually develops rather slowly and does not manifest itself for some time, usually being discovered only after it has produced general symptoms characterized by persistent fever, obscure abdominal symptoms and additional signs of encapsulated infection. Of all the signs and symptoms, fever is the most constant and reliable guide in diagnosis; it (the fever) is usually ushered in with a chill, is remittent in type, and because of this persistent elevation of temperature perinephritic suppurative processes are often confused with typhoid fever, ulcerative colitis, influenza, pleurisy, malaria and other infections. Pain is quite variable, usually of the constant, dull, nonradiating variety, located in the flank or

upper abdomen. In patients presenting second and third degree ptosis of the kidney, the pain is often confined to the abdomen, causing one to mistake perinephritic abscess for cholecystitis, appendicitis, salpingitis, pancreatitis, splenitis, hepatitis, and other abdominal conditions. In some cases the pain in the renal area is rather sharp and may radiate to the abdomen, umbilicus, scrotum, or shoulder. Gastro-intestinal symptoms consisting of nausea, vomiting and constipation are quite common. Leucocytosis is quite constant and varies between 10,000 and 35,000. Fullness of the loin or abdomen is an important late diagnostic sign. The swelling is usually associated with the kidney and does not move with respiration or with changes of posture. It is well to make measurements from the umbilicus to the spinal processes in order to detect this fullness, and this observation sometimes demonstrates swelling which is otherwise not apparent on inspection. Tenderness in the costovertebral angle, spasm and rigidity of the overlying musculature, congestion and reddening of the superficial skin, occur only after the abscess has attained large proportions, at which time it presents little difficulty in diagnosis. (Fig. 1.) We favor a complete urological examination, except in the occasional case in which it is contraindicated, and agree with Ockerblad, Braasch and others that it should always precede operative interference. There is a paucity of urine findings as compared with the severity of the illness. The urine usually shows a slight trace of albumin, a few leucocytes and organisms and an occasional cast which one finds in generalized infections such as pneumonia, typhoid fever, influenza, etc. These rather negative urine findings have been emphasized by Rolnick and Burnstein. However, careful examination of the urine in which it is centrifugalized over a long period of time and subject to culture frequently reveals the offending staphylococcus. In 1911, Baum noted that staphylococci were recovered in the urine of six of his seven cases. The importance of these findings have been emphasized by Taylor, Floyd and Pitman, Day and the author, as well as by Baum. While the finding of staphylococci is of some value in arriving at a diagnosis, one must realize that they also occur in the urine of patients suffering from pyelonephritis, cortical abscess and renal carbuncle, therefore adding difficulty to the differential diagnosis. Needling for the purpose of withdrawing pus for diagnosis is condemned as it is not without danger, particularly if the abscess happens to be located in front of or above the kidney. I recall a patient, a woman, seen in consultation, who was suffering from a perinephritic abscess secondary to a boil in the gluteal region, in whom repeated punctures of the renal fossa failed to reveal pus and these were followed by blood in the urine. Ex-

Fig. 1. Schematic illustration of a sagittal section demonstrating different types of perinephritic abscess. Note (A) suprarenal type of abscess causing pressure on the diaphragm, (B) the retro-renal type producing bulging of the loin, (C) prerenal type resulting in displacement of the colon and (D) the infrarenal type extending caudad into the bony pelvis.

ploration of the lung failed to reveal an abscess. A subsequent lumbar incision was made and after considerable exploration, encapsulated pus was located anterior to the lower pole of the kidney. In attempting to tap the cavity with the needle, the kidney was needlessly traumatized. Fortunately this trauma was not followed by damage to the kidney.

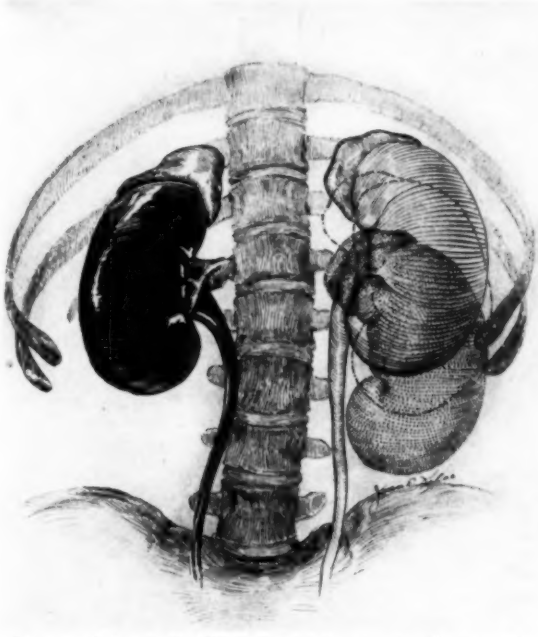

Fig. 2. Schematic illustration demonstrating renal fixation, the author's new positive roentgenographic sign for the diagnosis of perinephritic abscess. In making the standing retrograde or intravenous pyelogram one notes lack of normal renal mobility as demonstrated on the right side. On the left side one sees usual descent of the kidney varying from 2 to 10 cm. in the different positions in which it is usually situated.

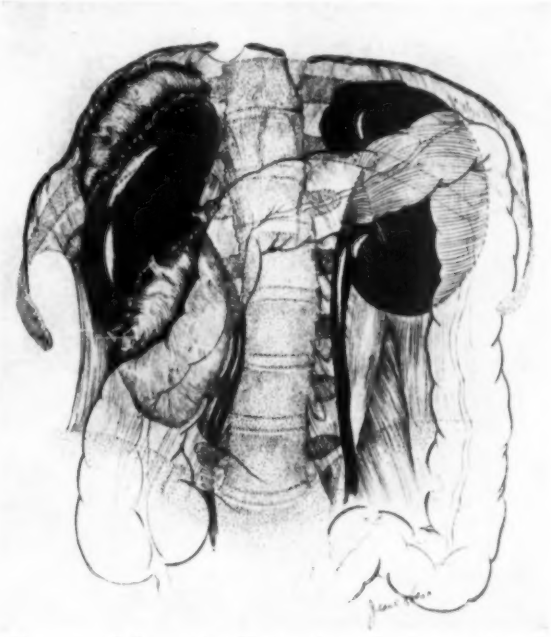

Fig. 3. Schematic illustration demonstrating other positive roentgenographic signs of perinephritic abscess. On the right side note: obscuration of the lateral border of psoas muscle, of kidney outline, ribs and lateral processes of the spine, shadow due to the abscess itself, outward displacement of kidney and inward displacement of ureter, curvature of the spine with concavity on side of abscess, convexity away from abscess and approximation of last rib with crest of ileum, displacement of colon, upward displacement of diaphragm.

ROENTGENOGRAPHIC SIGNS

All investigators of perinephritic abscess agree that the *x*-ray signs of suppurative perinephritis are only of value when studied in connection with the history, clinical course and the presence of the classical general signs and symptoms and special urological findings. These signs may also be produced by kidney lesions, disease of the neighboring abdominal organs, and inflammatory conditions of the nearby muscular and skeletal structures making up the renal fossa. A collection of gas in the gastrointestinal tract which is so often present and secondary to the infectious process in the perinephrium often obscures these roentgenographic signs. Therefore in employing the *x*-ray for diagnostic aid, one should attempt to eliminate this masking accumulation of gas by the previous oral administration of castor oil and the employment of enemas, and one should make repeated *x*-ray studies over a period of days.

The roentgenographic signs are enumerated in order of their constancy, frequency and importance. They consist of:

1. The author's new sign of renal fixation determined by making retrograde and intravenous pyelograms in the horizontal and standing posture. (Fig. 2.)

2. Obscuration of the lateral border of the psoas muscle, of the kidney outline, the

ribs and lateral processes of the spine. (Fig. 3.)

3. Shadow due to collection of pus in the abscess.

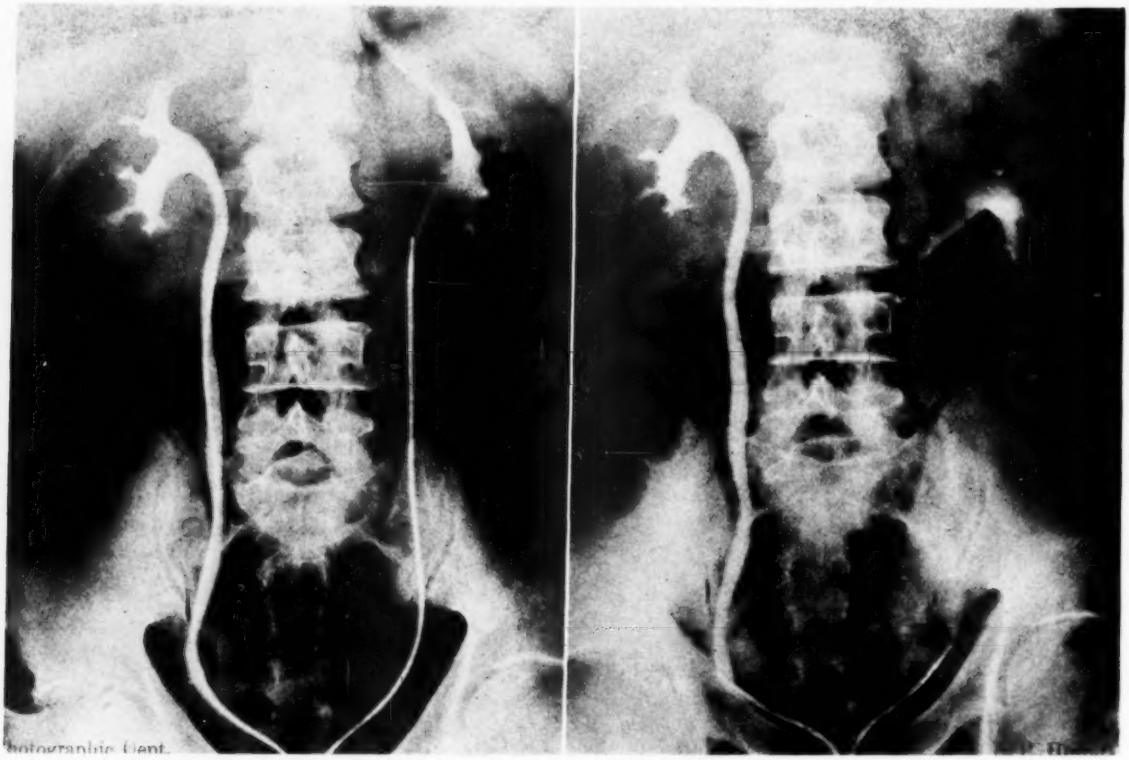

Fig. 4a. Horizontal pyelogram of male, aged 38, presenting fever, leucocytosis, bulging of loin, pain and tenderness of right kidney. Pulmonary embolism confused the clinical feature.

Fig. 4b. Vertical pyelogram of same patient, demonstrating author's new roentgenographic sign consisting of renal fixation.

4. Outward displacement of the kidney and inward displacement of the ureter determined by taking sterioscopic films.

5. Curvature of the spine with convexity away from the abscess.

6. Displacement of the colon.

7. Displacement and fixation of the diaphragm.

8. Fluoroscopic signs consisting of dis turbance of respiratory synchronism and the visualization of a wave in the pus cavity produced by shaking the patient.

9. Injection of the abscess cavity by opaque media.

1. *Renal Fixation, Our New Roentgenographic Sign for Diagnosis of Perinephritic Abscess.* Lack of renal mobility occurring in perinephritic abscess is determined by making retrograde and intravenous pyelograms in the horizontal and standing position, and is the result of twenty years intensive study of renal mobility. (Figs. 4*a* and 4*b*.) A detailed perusal of the American and foreign literature fails to reveal a previous description of this *x*-ray sign. The discovery of renal fixation occurring in perinephritic abscess was first described by the author in a monograph published on Movable Kidney in 1925 and in a number of publications since that time. This observation was based on a study of twenty-seven cases in which a complete urological examination had been made and it has been repeatedly corroborated at operation and at autopsy; it occurs early and is always present. Indeed, as soon as the septic emboli lodge in the end arteries of the perirenal fat contained in the perinephrium, setting up local foci of infection, the resulting inflammatory processes quickly cause adhesions between the kidney capsule and the surrounding fat causing fixation of the kidney to the perinephritic

tissues. A case illustrating the extremely early fixation occurring in perinephritic abscess was observed through the courtesy of Dr. Wm. Frey who referred a toxic young girl, aged 9, suffering from remittent fever and pain and tenderness in the left abdominal quadrant. There was a history of a boil on the hand some ten days before. The leucocytes were increased in number, the urine was negative except that it contained a few staphylococci. Urological examination revealed some swelling and tenderness of the left lumbar and upper abdominal region with rigidity of the overlying musculature. Cystoscopic examination was essentially negative except that the left kidney had lost its mobility, as ascertained by making a pyelogram in the vertical posture. Lumbar incision was made and to our surprise no frank pus was encountered. The perirenal tissues, however, presented extensive congestion and edema. A drain was left in place—drainage of pus followed in a few days with a drop in fever and disappearance of other symptoms. There we knew we had intervened during the very first stage of the inflammatory process even before pus had formed.

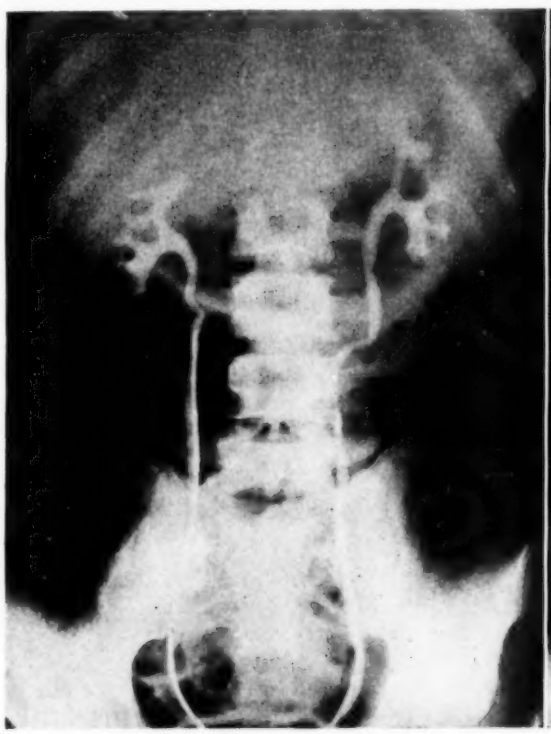

Fig. 5A. Horizontal pyelogram of male, aged 21, presenting fever, leucocytosis, pain and swelling and tenderness in right upper abdomen occurring after prostatic abscess.

Fig. 5B. Vertical pyelogram: spacity due to irritation of neighboring abscess has caused most of the pyelographic fluid to run out of the kidney. The renal mass, however, being firmly fixed, has lost normal renal mobility. At operation, a prerenal abscess was encountered high up in the kidney fossa and relief was obtained by drainage.

There are certain technical points which must be rigidly carried out in order to detect the author's sign. Pyelograms must be made in the Trendelenburg, horizontal and vertical positions and sometimes the lateral and ventral as well. It is essential that the compressing band, commonly used in conjunction with taking films with the Potter-Buckey diaphragm, should be released when the patient is placed in the standing posture. This point is sometimes overlooked, with the result that an unanchored kidney might be prevented from making its downward excursion, and this could lead to an erroneous conclusion.

To eliminate this possibility, we support the patient in the upright posture by the use of a second band that is attached to the upper portion of the table and extends in front of the chest. We require the employment of tables on which the patient can be raised upright, not the semi-reclining position. After the patient has been hoisted to the standing posture, he is asked to breathe deeply a few times in order to give the kidney a chance to descend, provided it is not anchored in place. The film is then taken after the patient has exhaled. It is our custom to locate the position of the kidney by comparing the position of the lower or upper major calyx with a given point on the opposite vertebra. In cases of perinephritic abscess, the kidney is found to be anchored in place at a certain level, and it does not move in the Trendelenburg position or in the upright posture. The major calyx will remain at the same level, as compared to a given point on the vertebra situated opposite to it, when the film is taken in the Trendelenburg and horizontal positions. If the technique is properly carried out, this renal fixation sign will be found to be constant and is of definite value in arriving at a correct diagnosis. (Figs. *5a* and *5b*.) It is also present and of value in the diagnosis of non-suppurative perinephritis, renal carbuncle and cortical abscess. The absence of the roentgenographic fixation sign is negative proof of perinephritic abscess. A case in point is a young man 17 years of age, referred to us for investigation with the diagnosis of perinephritic abscess. He was suffering from remittent fever, pain and tenderness in the left upper abdomen and lumbar region. There was a history of a boil over the knee some two weeks before. Leucocytosis was 19,000 and the urine contained pus and staphylococci. Urological examination revealed swelling and tenderness in the left lumbar and upper abdominal region with rigidity of the overlying musculature and a few pus cells and staphylococci in the left kidney urine. In making the pyelogram

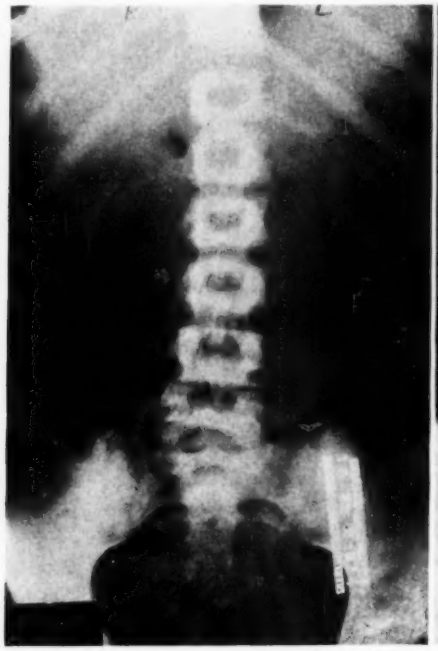

Fig. 6. Roentgenogram of a girl, aged 13, presenting perinephritic abscess secondary to solitary cortical abscess of lower pole of right kidney occurring after a stye in the eye. Note obscuration of kidney outline and curvature of the spine with concavity on the side of abscess and approximation of the lower rib to the crest of the ileum.

Fig. 7. Pyelogram of right kidney of same patient as shown in Fig. 6.

in the standing posture the left kidney was found to make an excursion of 5 cm. We ruled out perinephritic abscess: the boy's pyelonephritis was relieved by renal lavage.

2. *Obscuration of the Lateral Border of the Psoas Muscle, the Kidney Outline, Ribs and Lateral Processes of the Spine.* This phenomenon was first observed by Alexander in 1912 and described by Révész in 1928. (Figs. 6 and 7.) It is considered to be a most important sign, by Brunn and Rhodes (1930) Ringler and Manson (1931) etc. Unfortunately, roentgenograms are not always clear because of the accumulation of gas in the gastro-intestinal tract. This phenomenon occurs frequently on the right side and has been called "hyper-pneumocolie" by Porcher. Accumulation of gas on the left side is less frequent and more readily eliminated by catharsis. Obscuration of the lateral border of the psoas is due to the accumulation of pus or to edema associated with the abscess as many cases have been observed in whom the area of obscuration outmeasured the abscess cavity. Unfortunately, obscuration of the psoas shadow also occurs in abdominal tumors, retroperitoneal neoplasms, appendicitis with perforation and in many renal lesions such as tumor, hydronephrosis, lithiasis, polycystic kidney, etc. and may therefore lead to confusion. The abscess cavity and its associated edema causes obscuration of the ribs, lateral processes of the spine and the kidney itself. The loss of a clean-cut kidney outline suggests abscess formation. On the other hand, a well defined kidney outline, the "signe de clivage" of Porcher, is of great negative significance. Following the roentgenographic sign of fixation of the kidney, obscuration of the psoas shadow is of the next importance. Unfortunately it does not occur early and takes place about one to two weeks following the formation of the abscess.

3. *Roentgenographic Shadow of Abscess.* The diagnostic importance of the shadow cast by the abscess itself was emphasized by Koll (1913) who considered it of most great importance. Doberauer (1915) and Laurell (1921) called attention to its diagnostic significance particularly when compared with the opposite normal side. The opacity of the abscess varies with the thickness of collection of pus and the transparence of the area in which it occurs. In an organ containing a medium as transparent as that of the lungs, a small abscess can be readily visualized; on the other hand, a rather large abscess in the perinephrium can be masked by a highly vascularized viscus such as the colon filled with gas. The presence of bubbles of gas in the shadow cast by the abscess is of great significance.

4. *Outward Displacement of the Kidney and Inward Displacement of the Ureter Observed by Taking Stereoscopic Films.* In 1926, A. R. Stevens reported the outward displacement of the lower pole of the kidney resulting from a perinephritic abscess secondary to a ruptured diverticulum of the upper ureter. The accumulation of pus in the perinephrium, causing outward and lateral displacement of the kidney as well as inward displacement of the ureter, causing it to curve like a taut bow, observed by taking stereoscopic films, was described by Peacock in 1929. He observed this phenomenon in ten of the eighteen cases that he reported. Unfortunately, displacement of the kidney and ureter is absent in the supra and prerenal types of abscesses and this valuable sign is of no value in these types of abscess.

5. *Curvature of the Spine with Convexity Away from the Abscess.* This phenomenon was first observed by Alexander in 1912. In 1926, Carty observed its presence in perinephritic abscess as well as in lesions of the lung and kidneys. It was emphasized by Beer, Lipsett and Friedman in 1928, by Brunn and Rhodes in 1930. The curvature of the spine is due to psoas spasm, in which the convexity is away from the side of the abscess. The concavity is seen on the affected side causing approximation of the lower ribs with the crest of the ilium. It also occurs in trauma and infection of the spinal muscles, pleural effusion, renal stone

(positive in 60 per cent of 100 cases studied by Carty), hydronephrosis, etc. Although of some assistance it is inconstant and has

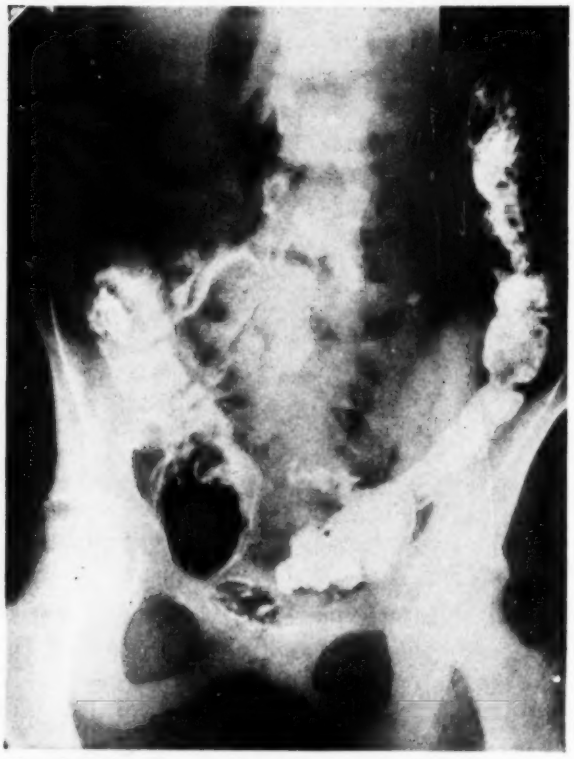

FIG. 8. Film of gastro-intestinal tract of same patient as shown in Fig. 6 after ingestion of barium: showing mesial and caudal displacement of colon.

been even termed misleading (Porcher). (See Fig. 6.)

6. *Displacement of the Colon.* Displacement of the colon can sometimes be detected in taking a plain film in which the accumulated gas within this viscus so often accompanying perinephritic abscess visualizes the displaced large intestine. It occurs rather late and is only seen in prerenal and infrarenal abscesses after they have attained considerable size. This sign is also obtained by utilizing the barium enema. (Fig. 8.)

7. *Displacement and Fixation of the Diaphragm.* Displacement of the diaphragm occurs in the suprarenal type of abscess and in huge pre and retrorenal types. This phenomenon was emphasized by Pancost (1920) and Fritz (1928). When present, it is of great significance. Unfortunately it is absent in infrarenal and the smaller type of retro and prerenal type of abscesses.

8. *Fluoroscopic Signs.* Under the fluoroscope one sometimes observes diminution or limitation of the diaphragmatic excursion, more marked on expiration. One is able to observe an interference with normal respiratory synchronism in which expiration is found to be inhibited or absent and inspiration remains normal. While observing through the fluoroscope, a definite wave passing over the surface of the pus cavity might be obtained by vigorously shaking the body of the patient. Pancost reported two such cases in 1920 and Fritz emphasized this point in 1928. It is understood that this phenomenon is observed only in large advanced abscess formation.

9. *Injection of the Abscess Cavity by Opaque Media.* In mentioning this sign, we wish to condemn the employment of the blundering, traumatizing, diagnostic exploratory needle as a means of diagnosis of perinephritic abscess. Feci (1928) injected perinephritic abscess with opaque media in order to visualize the abscess and determine its size and distribution. In post-operative perinephritic abscess, injection of the fistulous tract is of great aid. Other than for the post-operative type of abscess, this procedure has not been generally utilized. (Table II.)

TABLE II

FREQUENCY OF POSITIVE X-RAY SIGNS OF 27 CASES

Renal fixation	27
Obscuration of psoas	17
Shadow cast by abscess	12
Displacement of kidney and ureter	13
Curvature of the spine	15
Displacement of diaphragm	8
Displacement of colon	8
Injection of abscessed cavity	3

TREATMENT

The treatment of perinephritic abscess dates from the time of Hippocrates who, as early as 460 B.C., chronicled his daring operations on the kidney and in referring to perinephritic abscess advised, "as soon as a swelling has appeared in the region of the kidney, one should incise it down to the kidney." The treatment of suppurative perinephritis can be divided into (1) pro-

phylactic and (2) surgical. Treatment is rather different in dealing with the metastatic hematogenous type of abscess, in treating suppurative perinephritis associated with renal lesions and in handling paranephritic abscess secondary to extraneous inflammatory lesions.

1. *Propbylactic.* In reviewing the extensive literature dealing with the treatment of suppurative perinephritis we were surprised to learn that its prophylactic treatment has been entirely neglected. We emphasize the importance of such prophylactic treatment and advise wide early surgical drainage of staphylococcic skin infections such as boils, furuncles, carbuncle, peronychia, etc. thereby minimizing the chance of hematogenous invasion by staphylococci present in these lesions. We recommend early prostatotomy for prostatic abscess due to staphyloccus invasion. I recall a young man who presented a huge prostatic abscess from which numerous staphylococci were recovered. Prostatotomy was advised. He improved to such an extent following pressure massage that surgical drainage was not carried out. A short time later his remittent fever, leucocytosis, etc., returned with the addition of tenderness and pain in the upper right abdomen. Fixation of the kidney was observed in taking a vertical pyelogram and at operation a prerenal abscess situated quite high was encountered. There is little question that, had prostatotomy been performed early, the metastatic perinephritic abscess would not have occurred. Infections in the tonsils, sinuses and middle ear should be cleared up with the object of preventing metastatic infection of the perinephrium. We also recommend the oral administration of methyline blue, prontylin and the oxides of tin, both of which have a specific bacteriocidal action against the staphylococcus. The use of these drugs in acute staphylococcic inflammatory foci often prevent later metastatic manifestations in the perinephrium and in other remote portions of the body.

Certain prophylactic measures consisting of proper drainage of kidney wounds will prevent the great majority of the post-operative type of perinephritic abscess which may follow interventions on the kidney. We advise pyelotomy drainage in pyelo and nephrolithotomy. In dealing with pyonephrosis, kidney abscess and other inflammatory lesions of the kidney it is well to insert a drain in the superior and inferior portions of the renal fossa bringing them out through the upper and lower extremities of the incision. In removing a tuberculous kidney it is well to extirpate the perirenal fat which is sometimes infected with tubercle bacilli. In those cases in which it is not involved, it may become a future site of infection resulting in abscess formation which is usually quite resistent to treatment. Copious drainage in addition to removing drains, little by little, over a period of a week or ten days, lessens the frequency of post-operative perinephritic abscess.

The early diagnosis and prompt treatment of kidney lesions, such as tuberculosis, lithiasis, carbuncle, cortical abscess formation, etc., often prevent the formation of perinephric abscess. I recall a patient, a lawyer, presenting bilateral stone formation who emphatically refused operative relief. A calculus became impacted in the uretero-pelvic junction of the right kidney causing back pressure resulting in uroginous cortical infection and a huge suprarenal perinephric abscess. In January, 1929, I was obliged to perform an emergency operation, removing the stone and evacuating 1500 c.c. of pus from a suprarenal abscess which had ruptured into the lung by necrosis. Invasion of the lung lowered the resistence of this organ to such an extent that the patient developed pneunia three weeks later, from which he succumbed. There is no question in my mind that early removal of this stone by pyelotomy would have prevented the formation of the fatal perinephric abscess.

2. *Surgical.* A certain number of cases of inflammatory processes of the perineph-

rium undergo resolution spontaneously, causing no further symptoms to the patient or damage to the kidney. There is no question that cicatricial changes result from such resolution of the perinephritic infection causing a sclerosing perinephritis, but it is not within the scope of this paper to discuss the diagnosis and treatment of this interesting and illusive condition. During the early days of modern kidney surgery dating back to the latter portion of the nineteenth century, surgeons were wont to aspirate pus contained within the abscess by means of the exploratory needle. In 1880, Riverdin and Gaddy independently reported cure of perinephritic abscess by aspiration through a needle and the injection of carbolic acid. Even in later years, Kopp (1920) and Chwalla (1929) reported successful relief by employing aspiration. We concede that needling of an abscess could be employed in the treatment of the large retrorenal type of abscess. However this blind procedure is unsurgical in principle, and cannot be employed in the relief of the suprarenal, prerenal and infrarenal types of abscess without risk of injuring the kidney, the lung, the peritoneal cavity, including neighboring organs contained therein, with the added danger of spreading infection into the above mentioned structures, resulting in unpleasant complications. We recommend an exploratory lumbotomy in all cases with the employment of the usual sized curvo-linear kidney incision. Sufficient exposure permits one to search for walled off pockets, to examine the kidney for the presence of single and multiple cortical abscesses, renal carbuncle, etc. It assures adequate drainage of the abscess including walled-off portions that might be present, and permits one to institute proper drainage of cortical abscesses in those cases in which they are associated with perinephritic abscess. Early diagnosis and incision have been emphasized by Gibney (1880) Eisenstaedt (1929), Crenshaw (1932) and many others. Wide exploratory incisions have been recommended by Nieden (1878), Pugh (1925), Fowler and Dorman (1931), Scholl (1933), Rusché and Bacon (1935) and many others. We recommend an incision with sufficient exposure to permit exploration of the kidney and the entire renal fossa. We advise copious drainage employing cigarette drains or the petrolatum gauze type and removing a little of the packing each day, so that the abscess cavity will heal from the bottom. We advise against the common practice of removal of the entire drain in twenty-four to forty-eight hours because the superficial portion of the wound often heals allowing the original abscess to reform, often in much larger proportions than the original abscess. We withdraw the drain little by little each day usually taking ten to fourteen days for its entire removal.

In dealing with perinephric abscess secondary to inflammatory kidney conditions which have destroyed this organ and in which nephrectomy is indicated, we advise the two stage operation. The first stage consists of drainage of the perinephritic abscess. After toxic symptoms have become minimized and the patient's general condition strengthened, removal of the kidney is employed, usually ten days to two weeks following the first intervention. In 1934, I operated upon a woman with a huge infrarenal perinephritic abscess associated with pyonephrosis. In debating whether or not to remove the kidney, nephrectomy seemed so easy that the kidney was expediciously removed in order to spare our patient a second intervention. Death followed in five days. I firmly believe that, had the operation been performed in two stages, in this case, the patient would not have succumbed. On the other hand, we have successfully cured a number of desperately ill patients with perinephritic abscess secondary to advanced inflammatory processes of the kidney including calculous pyonephrosis, tuberculosis, spontaneous and traumatic rupture of the kidney, by two stage nephrectomy. These patients seem moribund at the time of the first stage drainage operation, usually performed under local

anesthesia, but it is astonishing to see how rapidly they increase in strength, permitting subsequent nephrectomy with less hazard. In certain cases of perinephritic abscess associated with acute hemotogenous multiple abscess of the kidney so well described by Brewer, one should not wait too long before performing the second stage nephrectomy because scepticemia may take place in the interim, resulting in death. Rochet reported such a case in 1924, in which death occurred in a patient with whom an interval of three weeks elapsed between the first and second stages. In such cases it is best to perform the second stage nephrectomy within seven days.

MORTALITY

The mortality in connection with perinephritic abscess is still quite high. This should act to stimulate the urologist to acquire a thorough understanding of the four general types of perinephritic abscess. Treatment varies with the type, origin of abscess, etc., and accurate knowledge of the pathological conditions present assures successful treatment with minimum mortality in the latter part of the nineteenth century, in the pioneer days of modern renal surgery, was well exemplified by Nieden (1878) who reported a mortality of 50 per cent, the usual death rate following all surgical interventions on the kidney at this time. Later Kuster reported mortality of 16.79 per cent, Miller (1910) 14.3–10 per cent, Hunt (1927) 6.6–10 per cent, Ockerblad (1927) 20 per cent, and Campbell (1930) 20.4–10 per cent. Our mortality was nil in treatment of the hematogenous type of perinephritic abscess and 8.3 per cent in the perinephric type secondary to renal lesions. A complete urological study of all personal cases, scrupulously carried to a scientific diagnosis of the particular type of abscess present (hematogenous metastatic, perirenal and paranephritic) has enabled us more intelligently to treat our cases with resulting lowered mortality. It is interesting to note that many advanced cases reported in the literature entirely escaped detection during life and were finally diagnosed on the autopsy table. We advise complete urological investigation on all patients in whom perinephritic abscess is suspected except in those in whom extreme debility or prostration would not warrant it. By virtue of such complete studies, many obscure cases will be solved, treatment instituted early, mortality lowered and fewer cases diagnosed on the operating and the autopsy table.

CONCLUSIONS

I. A new valuable roentgenographic sign for the diagnosis of suppurative perinephritis is presented. It consists of renal fixation evidenced by making retrograde or intravenous pyelograms in the standing position. This sign occurs early, is present in all cases, and has been repeatedly verified by operation or by autopsy. It was the only positive X-ray sign encountered in twenty-seven proven cases of perinephritic abscess in which a complete urological examination was made.

II. (1) The early diagnosis and intelligent treatment of suppurative perinephritis depends upon a thorough knowledge of all types. We classify them as follows:

1 (a) primary hematogenous, metastatic type secondary to staphylococcal foci elsewhere in the body consisting of infections of the skin, bones, tonsils, prostate gland, etc. with trauma playing the rôle of lowered resistance because of contusion or infection of hematoma (b) hematogenous type of same origin secondary to abscess formation of the renal cortex.

(2) Perinephric abscess secondary to kidney lesions: pyonephrosis, tuberculosis, lithiasis, infected polycystic disease, spontaneous and traumatic rupture, inadequate drainage of kidney wounds, etc.

(3) Paranephritic abscess secondary to lesions of neighboring organs such as the lung, adrenal gland, abdominal and pelvic organs, infections of the skeletal and muscular structures forming the renal fossa, etc.

III. Important signs and symptoms are: persistent remittent fever, leucocytosis, fullness in the loin or abdomen with relative paucity of urine findings.

IV. Corroborative roentgenographic signs are: renal fixation, obscuration of the psoas muscle and kieney outline, displacement of the kidney and ureter revealed by stereoscopic films, opaque shadow cast by abscess, curvature of the spine, displacement of the colon and fluoroscopic evidence of disturbance of respiratory synchronism and the presence of a wave in the abscess cavity.

V. Treatment of perinephritic abscess consists of prophylactic measures instituted to relieve infectious processes of the skin, bone, prostate gland, throat, etc., in order to prevent invasion of the blood stream and later metastatic infection of the perinephrium. We recommend surgical drainage with sufficient exposure to permit search for walled off pockets, examination of the kidney for cortical abscess formation and adequate drainage. We advise two stage nephrectomy in grave cases of perinephric abscess secondary to destructive inflammatory processes of the kidney.

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THE MANAGEMENT OF PYELITIS IN PREGNANCY*

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THE increase of knowledge concerning urinary tract infections in pregnancy during the last two decades has established, on a reasonably definite basis, adequate treatment to control pyelitis in pregnancy, with safety to the mother, and a pronounced reduction in fetal loss of life. It has most certainly established as a fact that the measures which are suitable to the non-pregnant are only in part applicable to the pregnant woman. Also, an understanding of the anatomical, physiological and general systemic changes which accompany pregnancy is necessary if the pregnant woman is to be protected from that morbidity and loss of life which maintained in earlier days, and fetal mortality is to be kept low. In the three years, 1934, 1935 and 1936, at the Boston Lying-In Hospital where there were 7881 deliveries, there was a total loss of life of twenty-five mothers with no deaths from urinary disease. There was one kidney sacrificed during pregnancy in that period of time. There were no mothers whose morbidity required a stay in hospital because of urinary disease beyond thirty days. Loss of fetal life because of miscarriage or interruption of pregnancy for uncontrollable urinary tract infection shows a rapidly falling curve. It is not to be expected that fetal loss of life can be eliminated, since a severe pyelitis will occasionally result in a prompt miscarriage. There are also those rare fulminating infections in which induced labor may be indicated if maternal life is to be preserved.

Ideal management of pyelitis in pregnancy would imply a previous knowledge of the individual case beyond what is usually available. Symptomatic pyelitis in pregnancy, which appears oftenest in the third trimester, has nothing in it to indicate whether it represents an initial immediate infection, an exacerbation of pre-existing infection, an exacerbation of an uncured infection which has persisted from a previous pregnancy, or whether the kidneys were normal at the beginning of pregnancy or were already pathological. Inasmuch as it has not been possible to date to have such complete data on all our clinic cases, we have resorted to the institution of forced fluids throughout all the prenatal clinics. We advise fifteen glass intake of fluids daily in all pregnant women. The theory behind this measure is that clearance of fluids from the kidneys in pregnancy is impaired.

Intravenous pyelography in animals (Rossi[1]) shows that the non-pregnant rabbit produces the best pyelography in the fourth and fifth minute after injection of the dye. In rabbits which are in the fifteenth to twenty-fifth day of their pregnancy, the best plates are obtained at fifteen to twenty minutes after injection of the dye. The same is true of pregnant women. In the non-pregnant or in the first trimester of pregnancy the best intravenous pyelogram is shown from five to fifteen minutes after injection of the dye. After the first trimester there is delay in distribution of the dye throughout the retained urine in the pelves and ureters, although there is evidence of adequate excretion from the kidney tissue. Calyces fill promptly with concentrated dye. The best pyelography is obtained at thirty minutes in the average case. In extreme degrees of dilatation, the best distribution of the dye will not appear for as long as an hour to an hour and a half after injection. Such delay in clearance is undesirable when infection intervenes. The

* From the Urological Clinic of the Boston Lying-In Hospital.

tendency of patients with fever to decrease the output of urine and approach suppression, the added factor of decreased intake of fluid because of nausea which leads to further diminution of volume of urine, and the accumulation of pus in the retained concentrated urine rapidly produced the profound toxicity of these cases with which we are all familiar. Practically, forced fluids has proved beneficial. If infection intervenes, there is already good interchange of fluid, concentration is less marked because of adequate body fluids to insure continued excretion of urine, and toxicity does not occur so rapidly as it does in the dry patient. Since the introduction of wide use of forced fluids, we have not decreased the number of infections which occur, but have decreased their virulence. It is not uncommon to have patients appear in our out-patient clinic who show infected urines and give a history of having been febrile for two or three days at home, after which the fever subsided, they felt well again, and on appearance at the prenatal clinic have been referred to the urological clinic for further care. Also, those cases which continue febrile and are deemed to require admission to the hospital, remain less toxic and more frequently subside on expectant treatment than did those patients who had been carried on less fluid intake.

Forced fluids has not produced any untoward effects in the average case. There has been no evidence of increased edema noted by the obstetricians. The patients have remained healthy and comfortable. In patients with cardiac lesions such treatment may be contraindicated. The cardiac clinic feels sure that in a few cases increased fluids to control infection has been a factor in producing cardiac decompensation.

The significance of fluid balance in pregnancy is not yet adequately established. There is evidence to indicate that the peak capacity of the kidneys to handle water declines progressively among clinically normal pregnant women in the last twelve weeks of pregnancy (Janney and Walker[2]).

TREATMENT

Patients with infections of the upper urinary tract in pregnancy should be divided into two classes, those in the first trimester of pregnancy and those after the first trimester. The basis for this division is the appearance by the end of the first trimester of the effect of endocrine action on the kidney and ureter and the beginning of uterine pressure against the ureters to produce significant degrees of stasis in the upper ureter and pelvis. The former group are more amenable to treatment and may be cured of the infection by modern antiseptic measures. The latter group can seldom be cured of its infections during the pregnancy. Unfortunately, most infections appear from the fifth month of pregnancy on. There are certain types of infected cases which appear in the first trimester which should be considered as treatment problems. They can often be cured and the pregnancy proceed as an uncomplicated pregnancy after cure has been accomplished.

These early pregnancy infections may be considered under the following headings:

1. The rare case of onset of infection in the first trimester of pregnancy. Such cases do occur but are not common.

2. Persistent infections of pyelitis of infancy and childhood. I have collected but six established cases without gross pathology.

3. "Marriage bed infections." These constitute a considerable group. Pregnancy is apt to occur before the cystitis and pyelitis have had time to recover.

4. Casual pyelitis which occurs within a few months of marriage or pregnancy. These cases are to be considered as routine pyelitises of the non-pregnant which have remained uncured.

5. Persistent infections from previous pregnancies which have remained uncured between pregnancies. In this group one must keep in mind the causes for the failure of this group to recover spontaneously from its infections. Approximately one-third of

the cases show anaemias, cardiac, renal or other causes for debility. A second group show failure of the kidneys and ureters to undergo retrogression from pregnancy changes. A third group show gross pathology of the kidneys and ureters. And finally, bladder residuals from cystocele (Crabtree[3]).

In treatment of this group of first trimester infections establishment of a complete diagnosis by clinical chemistry tests, bacteriological studies, and intravenous or retrograde pyelography is essential. If the condition is acute and fever is present, I favor forced fluids and alkalinization throughout the acute stage and not antisepsis. Many of these cases are afebrile with acquired resistance to infection. Antisepsis can be instituted promptly in the latter cases and soon after the patient has become afebrile in the former group. Antisepsis has been employed in uncomplicated cases with almost uniform success in producing cures. It has not been thought safe to employ the Ketogenic diet in these women who already are usually suffering from nausea of pregnancy. Our chief reliance has been placed on acidification of the urine to a pH of 5.3 or under and administering hexamethylenamine, or better still, using Mandelic Acid. Through the liberality of Mallinckrodt Chemical Company, we have made use of Mandelic Acid in pregnancy cases. While it is, on the whole, unsatisfactory in cases of pyelitis of pregnancy which are beyond the fifth month of gestation, it is very effective in the early pregnancy cases. If the desired acidity is produced while a liberal intake of fluids is still being maintained, and the first day's administration of mandelic acid is given, the urine can then be concentrated without much danger of febrile response. The kidneys seem to produce proper concentration of the drug, and the residual urines in the pelves and ureters are not sufficient in size to nullify the effect of treatment.

Where there is found to be gross pathology in the urinary tract, residuals above 30 c.c. either in the bladder or renal pelves, or stones, there is not much likelihood of cure. The same applies to those cases of recent pregnancy in which retrogression of the pregnancy changes has not yet taken place.

In the treatment of infections by Mandelic Acid there seem to be two factors concerned: one, the virulence of the organism at the time treatment is instituted; the other, the acquired tolerance of the individual. In eight out of nine cases when the organism, taken direct from the urine, was planted in mandelated urine of the usual pH and Mandelic Acid concentration, it was killed. If it was passed through broth cultures in the interval while the patient was being treated by Mandelic Acid therapy until cured, and the culture planted in the mandelated urine on which the patient got well, after passing that urine through a Sietz filter, eight out of nine cultures grew in the mandelated urine. It has also been shown (Crabtree and Reich,[4] to be published elsewhere) that bacteria are more resistant to mandelated urine during the acute stage of an infection than either before or after the acute exacerbation. It has also been shown (Crabtree[3]) in multiple pregnancies, where infections persist throughout a series of pregnancies without cure having been established between pregnancies, that the initial pregnancy infection is usually febrile, and less than half of the subsequent pregnancies show marked febrile reactions. For this reason it seems to us unwise to attempt to treat intensively by antisepsis gross pathology or persistent pregnancy change cases, but rather to treat their exacerbations of temperature, if they occur, and allow them to finish that pregnancy before offering antisepsis, cystoscopic treatment or surgical relief. In this we are much more conservative than before the above facts were established. Where the condition is bilateral, or where a pyonephrosis is developing, interruption of the pregnancy should be done, and surgery promptly instituted. While surgery in the course of pregnancy

is proper, it is very difficult to make a proper estimate of the value of a kidney in the presence of pregnancy changes. The temptation is frequently to do nephrectomy in a type of kidney on which conservative measures are shown to be adequate after the pregnancy has been interrupted. On the whole, nephrectomy during pregnancy is inadvisable except in unusual cases. The removal of impacted ureteral calculus at any stage in pregnancy has always proved satisfactory.

Treatment of pyelitis in pregnancy in the second and third trimesters is not primarily aimed at cure. Within the last ten years we have industriously used most of the accepted antiseptic agents against control groups with almost equal lack of success. This record has been only slightly bettered by the use of Mandelic Acid. Our first enthusiasm for its value suffered by exclusion of the cases which were cured in the first trimester of pregnancy. So few remained of the second group which showed maintained sterile urines that I do not believe that treatment of the average pyelitis case, with average degree of dilatation of the pelves and ureters, is justified.

The aim of treatment should be to keep the infection from progressing beyond control until the patient acquires tolerance for it. The value of fluids in modifying the character of the infection has already been discussed. On admission of a febrile case into hospital, we maintain the fluid intake by clysis or intravenous administration of fluids, to as near 150 ounces as possible. Posture is important. The patient should at least be kept flat in bed on a low pillow, or with the foot of the bed elevated. Most of our own cases which have maintained fluid intake of reasonable amount throughout pregnancy subside symptomatically. Cystoscopic treatment is reserved for those who fail to recover or show from the start progressing symptoms. We are finding the need for cystoscopic management decreasing in the cases from our own clinic. Cystoscopic treatment in this clinic continues to consist of pelvic drainage only during the period of the cystoscopic treatment and cleansing of the distended channels by lavage. It is adequate, without the need for inlaying catheter, if employed early in the disease. I note, with interest, recent reports from clinics in which inlying catheters are extensively employed, that the number of nephrectomized patients far exceeds our figure of the loss of one kidney, in a clinic in which there were 7800 deliveries among which were included 300 urinary tract infections deemed suitable for hospital treatment over a three year period.

Alkalinization of the patient is the treatment of choice during the acute stage of pyelitis of pregnancy. I recognize no antiseptic or even bacteriostatic action from alkalinization. The unprofitable results from antisepsis in the latter portion of pregnancy have already been mentioned. Under alkalinization patients can maintain fluid intake, keep up sufficient intake of food to maintain the blood picture at somewhere near normal level, and are usually free from toxic symptoms. One of the most important factors in pyelitis of pregnancy, both as regards its inception, and continuance of symptomatology, is anemia. A loss of hemoglobin of 30 to 40 points and 1,000,000 to 1,500,000 red cells has been recorded in as short a period as seven to ten days of fever, nausea, and vomiting. This emphasizes the importance of diet, iron and other medications, and even transfusion as therapeutic measures for control of the incidence of pyelitis of pregnancy as well as for aid in the effort to acquire tolerance for the infection. Studies in the anemias of pregnancy (Minot and Swartz[5]) substantiate that view. Up to within the past few years, our obstetricians looked with disfavor on transfusions in pregnancy because of the possible deleterious effect upon the foetus. We now employ transfusion in these cases.

Once tolerance for the infection is acquired, the patients are returned to the outpatient clinic and kept under supervision whether they be routine cases or show gross pathology for maintenance of

fluid intake. Most patients require no medications. The majority of these patients maintain a reasonably clear urine. The appearance of unusual cloudiness of the urine, when fluid intake is maintained, is considered to indicate increased obstruction and a tendency towards pyonephrosis. Such cases are readmitted to hospital where rest in bed and occasionally cystoscopic treatment will usually restore them to ambulatory life. We do not wait for the appearance of fever in this group.

In that small group of patients which reach hospitalization in profound sepsis and debility, some are relieved by the above procedures. We have had no better success with inlying ureteral catheters. While an improvement in the condition of the patient may be obtained while the catheter is maintained in place, that improvement is apt to be lost on removal of the catheters, because of plugging with pus, or because of bladder discomfort which is often quite marked where the catheters are kept in place over a period of many days. The catheters must be maintained for long periods in these cases of profound sepsis, in most instances, because the condition of the patient is grave and recovery to the point of adequate tolerance for the infection is very slowly acquired. Nephrostomy drainage is much better if the pregnancy *must* be preserved. It is a measure which cannot be repeatedly employed without endangering the integrity of the kidney. It is easier to advise it for the first infected pregnancy than for subsequent ones.

The delivery of the patient with pyelitis of pregnancy, even though the infection is quiescent, precipitates the problem of the inadequate bladder and its management. In the non-infected cases, residual, uninfected urine, or retention does not offer the same risk of postpartum infection as does the infected case under the same circumstances. In the uninfected case palliation through the use of a catheter may be accomplished without much risk, for at least three to five days. In most cases in which catheterization has been employed in stubborn residuals postpartum infection has occurred five to ten days after delivery. Infection must be introduced into the bladder and cultured there before the postpartum infection results. In already infected cases retention or bladder residual development should mean immediate placement on constant drainage for a period of five days, and testing the patient for residual urine after the catheter is removed. If the residual exceeds two ounces the catheter should be replaced for a period of five days longer. Traut[6] and others have demonstrated the increased atony of the upper urinary tract following delivery, which is evidently of endocrine origin, and favors the postpartum infection. Theoretically, postpartum infections can be eliminated from obstetrics by perfect handling of the bladder after delivery. So far, none of us have achieved that goal. The uncertainty of fluid intake during long deliveries, the rate of excretion, even polyuria, after relief of obstruction by delivery and the presence of an enlarged soft uterus from which to demark the distended bladder through palpation have proved insurmountable difficulties. Large atonic overdistentions continue to escape detection.

The effect of delivery of the foetus on the progress of symptoms of pyelitis of pregnancy is of so gratifying a nature, that it continues to be mistaken for cure of the infection. In a recent study (Crabtree[3]) it has been shown that the peak of spontaneous recovery after pyelitis of pregnancy is in the second month after delivery. For some years we have arbitrarily set four months postpartum as the limit of watchful waiting. In the beginning we refrained from treatment up to this date in order that we might obtain a study group. Of late, antisepsis is begun as early as the end of the first month postpartum. The most effective antiseptics are hexamethylenamine in properly acidified urine, which is most commonly used because it is adequate for most of the cases. If it fails, mandelic acid is more

potent and clears many in which the former therapy has failed.

There remains a group of cases which appear both in the spontaneous recovery group and in the treated group in which infection is not cured at the end of four months. These are returned to hospital for investigation. The findings in this group are such as to indicate four classes of patients. The first consists of those women who either because of malnutrition, social reasons, or diseases such as cardiac disease, nephritis etc., maintain a subnormal state of health. The second group consists of those cases in which pregnancy changes persist beyond the four months limit. These cases will usually clear, if one waits long enough. The third group are cystocele cases with residuals above two ounces. Below that amount there seems not be be any variation from the normal rate of spontaneous recovery. Finally, the cases of gross renal pathology. We believe that it should be our aim to clear, by whatever means including surgery, our cases of infection between pregnancies and that the Lying-In Clinic does not discharge its obligation to the patient if it allows its patients to enter subsequent pregnancies with infection still present, gross pathology uncared for, or kidneys and ureters which have remained both dilated and infected from the preceding pregnancy. Somewhere in this conception must be found the reason for the preponderance of nephrectomies in women over men of which we have so long been conscious.

In operations on the kidneys of recently pregnant women, one should take into consideration the essential difference between the obstructive lesions which have their inception in the course of pregnancy, and chronic obstructive lesions (Crabtree[7]).

In the former group, the cause of the lesion has been endocrine relaxation of the musculature, distention and obstruction. Baird[8] has indicated already, and my own cases substantiated his view, that the dilated kidney and ureter in pregnancy is only stretched. I have collected and studied chronic obstructive lesions of the ureters and pelves, and find that these lesions appear to be the result of hypertrophy of musculature, atony and dilation when the peak of hypertrophy has passed, and whatever fixation change has occurred through fibrosis to limit indefinite distention. We are familiar with the reluctance of this latter group to return to normal. Some remain altered permanently. Lesions which are superimposed on the kidney and ureter of pregnancy have been found to return to normal within three weeks after obstructions of two and a half years, four years and one ten years duration. For this reason there is less cause for radical surgery in postpartum repairs on such a kidney and ureter than in chronic obstructive lesions of similar pyelographic appearance.

The relation of gross pathology, which appears to have antedated the pregnancy and renal abnormality, to pregnancy, exclusive of those conditions which appeared to us to have had their origin in the course of and due to pregnancy, shows that, on the whole, kidneys behave creditably during the child bearing period except for pyelitis infections. During the years 1930 to 1936, inclusive, there were 16,001 deliveries at the Boston Lying-In Hospital. Exclusive of study cases, which means, because of symptomatology, history of previous urinary disease, or question of other pathology besides pyelitis of pregnancy, including check up cases which failed to recover at the end of four months postpartum, approximately 300 cases have been studied urologically. In forty-four cases renal abnormalities or pre-existing pathology has been encountered. I say approximately 300 studies were made, because it is not clear in some instances whether interest in toxaemia might not have been the chief reason for renal investigation.

These cases might well be listed as an indication of a cross section of renal pathology in child-bearing women of an average age of 25 years.

Polycystic kidneys	1
Extreme ptosis	1
Reduplicated pelvis and ureters	8
Horseshoe kidneys	2
Congenitally small kidney	5
Ureteropelvic obstruction	8
Renal or ureteral calculus	6
Hydronephrosis with aberrant vessel	3
Hydronephrosis	5
Bilateral hydronephrosis	1
Tuberculosis	2
Pelvic kidneys	2
	44

Lesions below the brim of the pelvic such as ureterovesical abnormalities, bladder conditions and the patient with a single kidney, if that kidney was found to be normal, have been excluded.

There is no intention to indicate that renal abnormalities in so large a group of patients have always been picked up or that some patients with the pyelitis of pregnancy who were not sudied might not have shown pathology if investigated. It is not our practice to do studies including pyelography on routine cases of renal infection if the clinical course is satisfactory.

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Mandelic acid therapy is indicated in the treatment of the usual non-tuberculous urinary infections. When employed in infants, the physician must be especially alert to the onset of acidosis. For this reason, in all children, it is usually prudent to start with slightly less than average doses. From—"Pediatric Urology" by Meredith F. Campbell, M.D.

THE DIAGNOSIS AND INDICATIONS FOR TREATMENT OF RENAL TUBERCULOSIS

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MUCH has been accomplished during the past twelve years, not only by physicians and surgeons but by the general public, in the diagnosis and treatment of tuberculosis. Lay workers have learned how to apply measures directed at the prevention of this disease. They now understand the necessity of isolation of active cases and frequently report patients who have signs or symptoms usually associated with advancing phthisis. Medical officers have successfully practiced prevention and prophylaxis so that now they have to examine well persons if the control of tuberculosis may continue to advance. The use of tuberculin skin tests and Roentgen ray examinations of the chest may demonstrate incipient pulmonary lesions in apparently well persons when the ordinary physical examination reveals no diagnostic signs of this condition. By the use of similar methods we can now discover early lesions of renal tuberculosis before the patient has urinary symptoms.

During the last twenty years there has been a change, at least apparent, in the character of extrapulmonary lesions of tuberculosis. This is particularly true with the lesions that require surgical treatment. The resistance of individuals has been increased so that spread of tuberculosis from the chest cavity occurs with greater difficulty, and surgeons find these lesions more amenable to surgical treatment.

Today a *history* of genitourinary disease is not of much value in the diagnosis of the first or early lesions of renal tuberculosis. Formerly, the kidneys were not suspected until the patient began to complain of bladder irritability, frequency, hematuria, etc. Today we feel that if we wait until these symptoms appear, the kidney lesions are usually far advanced so that they may not be amenable to treatment. A history of previous pulmonary tuberculosis is important. A history of bone, joint or intestinal lesions is significant because this indicates that bacilli of tuberculosis have entered the blood stream from a focus in the chest. When this occurs, the kidneys should be suspected because with their profuse blood supply there is a good chance that emboli may be filtered out and renal lesions develop subsequently.

There may be no *symptoms* of a renal tuberculosis in its early stages. Hematuria occurs infrequently with early lesions. We believe that every patient with tuberculosis should be examined for renal infection before urinary symptoms are present. If all patients are subjected to a routine method of diagnosis and treatment, all lesions of renal tuberculosis may be discovered early and the majority may be arrested. If arrest is not possible by conservative methods, appropriate surgical treatment may be instituted before the lower urinary tract

becomes involved and other organs permanently crippled.

The frequently repeated examination of a sterile specimen of urine for tubercle bacilli is the only method of examination which will reveal positive findings that clinch the diagnosis of renal invasion. The normal kidney will not transmit bacilli of tuberculosis. Repeated interval examinations of the urine must be made because infected kidneys will transmit bacilli of tuberculosis, pus cells and blood cells into the urine at one time and not at another. The urinalysis practiced at Glen Lake Sanatorium, Oak Terrace, Minnesota, is as follows. All patients have routine studies of the urine every three months no matter where the tuberculous lesion may be located or its extent. If cellular elements are found in the urine, the sediment is stained by the Ziehl Nielson method. If no bacilli of tuberculosis are found, four weekly specimens, two of which are twenty-four hour collections, are centrifuged and the sediment is injected once each week into the peritoneal cavity of the same guinea pig. If more than occasional bacilli of tuberculosis are present, these should produce tissue reaction in the animal, and after six or eight weeks typical lesions may be observed in the glands and organs. In some instances the number of organisms may be small; the resistance of the animal may be greater than usual; or the organisms may have a low virulence so that lesions may not be produced. Subsequent injection of the sediment of additional specimens of urine may produce the disease.

The culture method of isolation of the bacilli of tuberculosis from the urine, which is less expensive, may be used instead of the inoculation of guinea pigs. However, this method requires several years of experience on the part of the laboratory worker in order to perfect technique. The results obtained by an experienced worker who uses the culture method are as good as, or better than, the animal method. A few positives may be picked up with the culture method that are missed with the guinea pig method and vice versa. Dr. McNabb of the Ontario Provincial Laboratories (who has done the most extensive cultural work to date) found more positives with the cultural method alone than with the guinea pig method alone in thousands of examinations. Petragini's culture media which consists of whole eggs combined with dye and blood media have been found to be the most successful.

At the Division of Preventable Diseases of the Minnesota Department of Health in Minneapolis, the culture method is used with all voided specimens of urine, as well as sputum. When catheterized specimens of urine are examined, part of the sediment is inoculated into one guinea pig and the remainder inoculated into culture media. In five years, the bacteriologists of the Minnesota Department of Health have found only one instance in which organisms isolated in cultures were non-virulent for guinea pigs.

Any patient with tuberculosis in any form *who shows cellular elements in the urine* should have a *complete urological examination*, including cystoscopy, whether or not bacilli of tuberculosis are found in the urine. After complete examination of the urine, functional tests should be done before cystoscopy is considered. Kidney function tests do not furnish a positive or negative diagnosis of early renal tuberculosis but they do give information as to the ability of the patient to withstand complete urological examinations, including bilateral retrograde pyelograms. These functional tests tell us *when* cystoscopy can best be done. The tests we most commonly use are the phenosulphonphthalein excretion test and blood chemistry studies, which include blood urea nitrogen, nonprotein nitrogen and blood creatinin. At the same time we obtain kidney, ureter and bladder roentgenograms. These films are not of great value in the diagnosis of early renal lesions of tuberculosis but they do reveal the old calcified type. They may also suggest the presence of psoas abscess.

When *cystoscopy* is attemped, it should be carefully performed. The reflux test

should be done to determine the possibility of contamination of the ureteral specimens of urine. This test is done by overdistending the bladder with a solution of methylene blue after the ureteral catheters are in place and before the cystoscope is removed. The urine that flows through the ureteral catheters is watched carefully for evidence of return of the methylene blue. If this is obtained, we know that reflux has occurred from the bladder up the ureteral lumen to the renal pelvis and back through the ureteral catheter. Reflux has been demonstrated in 14.0 per cent of our cystoscopies. This has occurred with all types of pathology and anesthesia.

When the reflux test is negative, indigo carmine may be given intravenously. This reveals a comparison of the gross function of the separate kidneys. We know that minor differences in the return of the indigo carmine do not necessarily indicate renal damage. Frequently kidneys with large destroyed areas of tuberculosis have no diminution of function. However, these findings are of value when considered in combination with other findings.

Subsequently 10–20 c.c. of urine are collected from each kidney pelvis. These specimens are taken to the laboratory at once, where a cell count of each is made. They are then centrifuged, the sediment divided and injected into two guinea pigs.

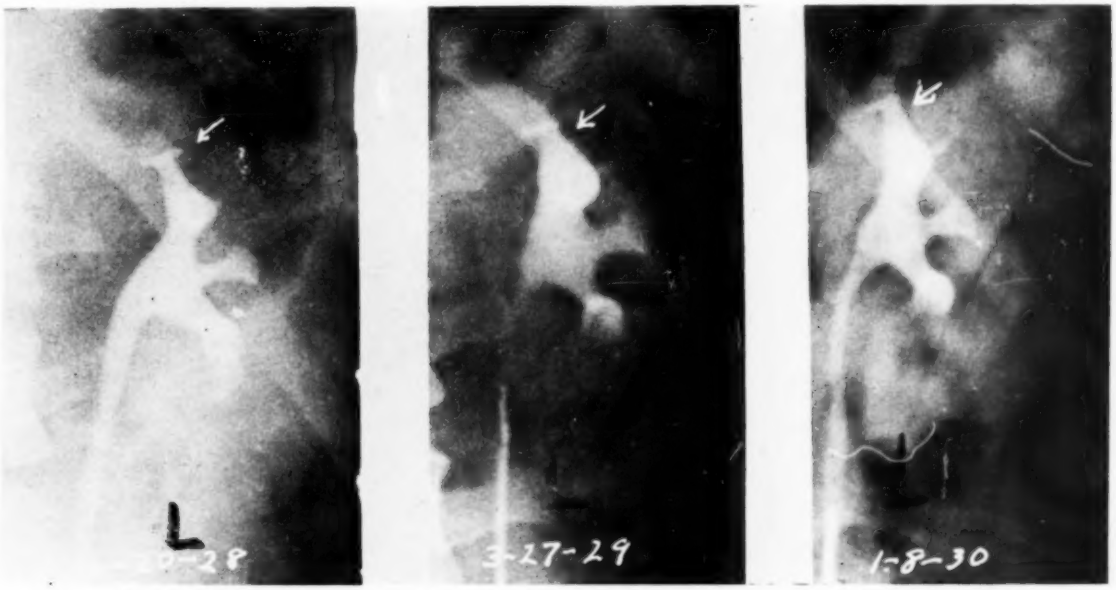

Fig. 1. Series of pyeloureterograms demonstrating parenchymal abscess type of renal tuberculosis.

These pigs are sacrificed at the end of six weeks. If the autopsy of the first pig is negative for lesions of tuberculosis, the second pig is allowed to live a second six weeks' period and then sacrificed.

We believe that *bilateral pyelography* is necessary before a complete diagnosis of the presence and extent of early destructive lesions of tuberculosis can be made. The practice of making repeated bilateral pyeloureterograms in renal tuberculosis has been criticised. We have made hundreds of bilateral pyelograms over a period of many years without evidence of spread of tuberculosis from the kidney. We have not observed miliary infection or meningitis as sequellae of retrograde pyelography. Ureteral catheters should be inserted so that their eyes are in the kidney pelves and not in separate calices or in the ureters. This arrangement permits withdrawal of the sodium iodide or whatever radio-opaque solution has been used as soon as the films are exposed. Two syringes are necessary to prevent cross-contamination of the specimens of urine obtained from the kidney pelves. We try to aspirate from each renal

pelvis the same amount of radio-opaque solution injected before pyeloureterograms were made.

There is always plenty of time available for careful study of the patient's urinary tract before surgical treatment is undertaken.

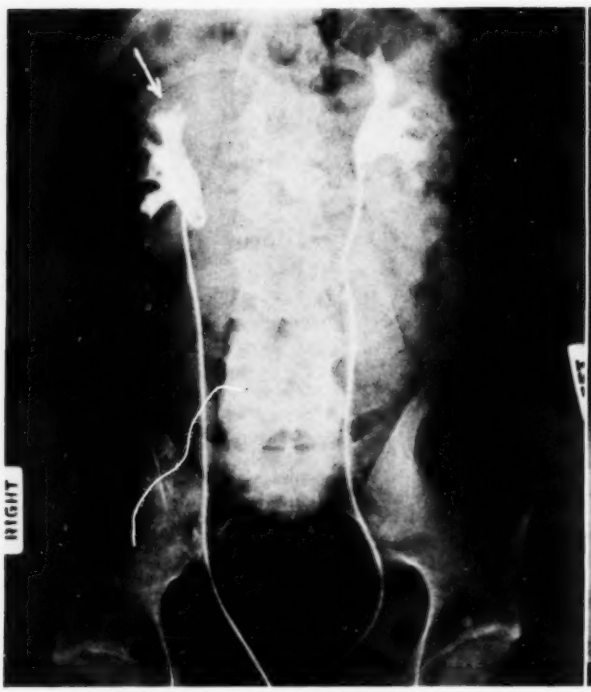

Fig. 2. Pyeloureterograms showing ulcerative type of renal tuberculosis involving the right kidney.

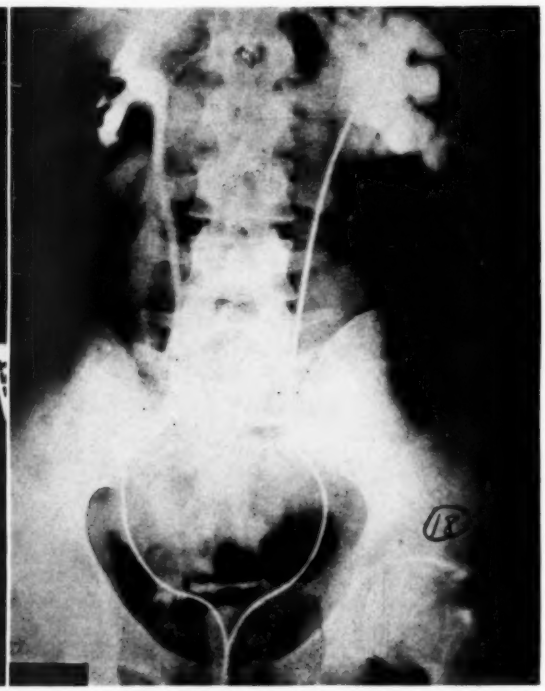

Fig. 3. Pyeloureterograms showing tuberculous pyonephrosis, left kidney.

We know of no method of examination that will reveal the tiny macroscopic ulcerative or destructive lesions of tuberculosis in the kidney parenchyma as constantly as the pyelogram. By this method we have been able to demonstrate small ulcerative lesions and parenchymal abscesses when a specimen of urine from the same kidney did not reveal bacilli of tuberculosis. Repeated bilateral pyelograms are necessary because if only one kidney is examined, the surgeon may overlook an unsuspected lesion in the other. The pyelogram has helped to estimate the relative amount of local defense against bacilli of tuberculosis as manifested by the kidney. If a patient has a good local and general resistance, a destructive tuberculous lesion may be held in abeyance or progress slowly. When the local defense and the general resistance are slight, the kidney may be destroyed quickly. These changes may be accurately followed only by pyelography. Repeated pyelograms reveal that a patient may have a destructive renal lesion of tuberculosis for months and years without demonstrable symptoms.

The intravenous method of urography has not been valuable in the diagnosis of the early or small destructive lesions of renal tuberculosis. However, this method of urography may furnish a positive but not a negative diagnosis of renal tuberculosis. It may not visualize the minor filling defects which may be observed with the retrograde method. Intravenous urography is most useful when it is impossible to cystoscope a patient or to catheterize both ureters. In these instances pyelography might be impossible without this method.

The lesions of renal tuberculosis that may be demonstrated in a well-filled retrograde pyelogram are the *ulcerative lesions, parenchymal abscess, and tuberculous pyonephrosis.* These can be *differentiated only by well-filled retrograde pyelograms,* which

will visualize any deformity of the kidney pelvis or parenchyma. The least destructive of these lesions, or the *ulcerative type*, phthisical areas may be surrounded by sufficient connective tissue so that they cannot, temporarily at least, connect with

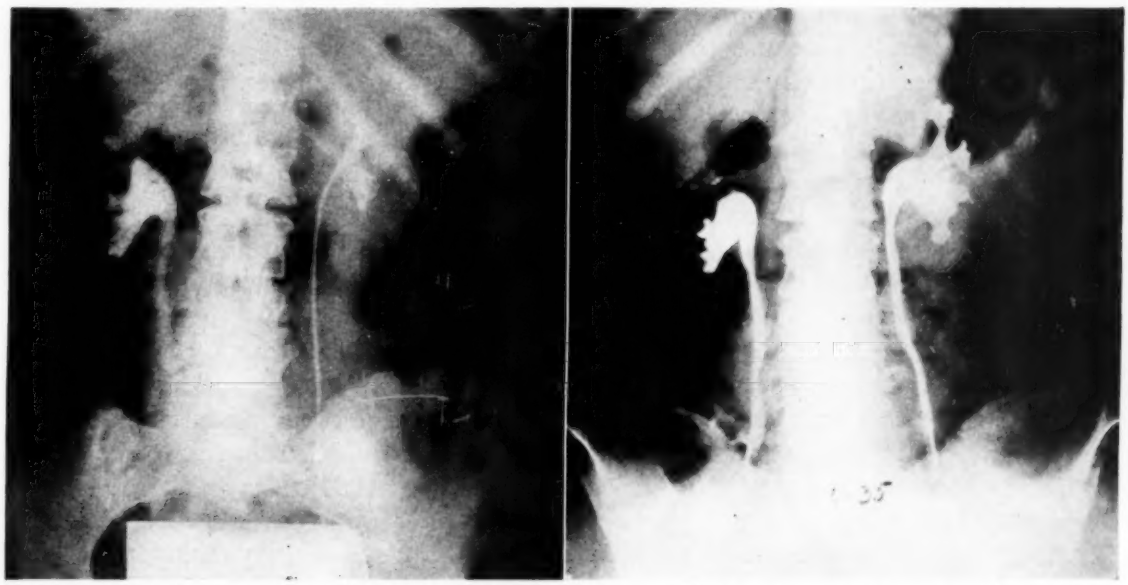

Fig. 4A. Pyeloureterograms showing bilateral renal disease (1924). Guinea pigs positive.

Fig. 4B. Pyeloureterograms, same patient as 4A, eleven years later, showing normal pelvic outline on the left and calcification in the upper pole of the right kidney. Guinea pigs negative.

appears in the pyelogram as a small irregularity or moth-eaten area in the border of a calyx. This projects slightly, if any, into the parenchyma. This defect may be so slight that a positive diagnosis may depend on its constant appearance in repeated retrograde pyelograms associated with the presence of pus cells and bacilli of tuberculosis in the urine.

The second type of lesion is the *parenchymal abscess*. In this, more destruction of renal tissue has occurred so that it is recognized in the well-filled pyelogram as a definite filling defect, projecting from the border of a calyx into the parenchyma of the kidney. Depending on the size of these lesions and the local efforts at healing, there may or may not be urinary symptoms. These lesions may be multiple and tissue destruction may progress rapidly to pyonephrosis. In most instances the local and general resistance is sufficient to hold an area of this type in check for many years. Small or moderate-sized abscesses or the calices or pelvis, preventing pus cells and bacilli of tuberculosis from reaching the urine from this source. They may not completely heal; however, one has been observed that did not progress for thirteen years and others have remained quiescent for shorter periods of time.

The third type of destructive lesion of renal tuberculosis we recognize is *tuberculous pyonephrosis*. This is the terminal stage of renal infection. It consists of multiple, extensive, parenchymal abscesses associated with widespread tuberculosis of the kidney pelvis. This type of lesion is the end-result of the two previously described. It follows undiagnosed and untreated renal tuberculosis occurring in a patient with little local or general resistance against the disease and extending over a considerable period of time. The pyelogram may be required in the diagnosis of this type of lesion but the destruction of the kidney is often so great that it is unnecessary. (Figs. 1, 2, 3 and 4.)

INDICATIONS FOR TREATMENT

We are making a study of the autopsy findings of individuals who died in Hennepin County with some lesion of genito-urinary tuberculosis. These reports are obtained from the Department of Pathology of the University of Minnesota. We are trying to determine how effective general and local resistance of patients can be in the arrest and control of lesions of tuberculosis in the kidney or kidneys. Can the local or general resistance become effective so that lesions of genito-urinary tuberculosis remain under control? And do we have to consider this defense a factor or *the major factor* when considering indications for treatment? Our study is incomplete; however, certain encouraging information is obtained.

We examined 17,777 consecutive autopsy reports and found 1,283 cases with some finding of tuberculosis. Of these 202 or 15.74 per cent had evidence of genito-urinary tuberculosis. There were fifty-five cases of unilateral renal tuberculosis. This was 4.28 per cent of the total number of cases examined and is the same figure obtained during a clinical study of the prevalence of renal tuberculosis in association with general tuberculosis. We found one case with a report of bilateral healed scars of renal tuberculosis. There were seventeen cases that showed evidence of tuberculosis of the prostate or epididymis, or both, without any gross evidence of renal tuberculosis. Unfortunately, there was no microscopic study of the kidneys in these cases so we cannot say positively whether a renal lesion existed. While tuberculosis can be carried to the prostate by the blood stream, we feel that in the majority of cases the spread of the infection is via the urine from the kidneys.

Our incomplete study of autopsy data and our clinical experience teach us that the first consideration in the determination of the treatment to be given any patient with renal tuberculosis is the estimation of his general condition and his or her ability to control lesions of tuberculosis. This defense against the bacillus tuberculosis must be manifested before any surgical treatment is recommended. We never forget that renal tuberculosis is a local manifestation of a general disease. It is rarely possible to extirpate all of a given individual's tuberculosis, so in general it may be stated that surgical treatment does not cure but is an aid in obtaining a good clinical result.

It is dangerous to attempt surgical treatment for renal tuberculosis in the presence of acute or recent pulmonary disease with the exudative types of lesions. Such radical treatment may cause an exacerbation of the disease and leave the patient in worse condition than before surgical treatment was attempted. The chronic fibrotic stages of the disease offer the surgeon a safer field for surgical treatment. However, there is always the possibility that any trauma which lowers the local or general resistance of the patient may be followed by a lighting up of a quiescent lesion locally or in some other organ. We have had one case of tuberculous meningitis two months following nephrectomy for renal tuberculosis. Dr. J. Harolde Turner reported a case of tuberculous meningitis following nephrectomy in the *Journal of Urology* for September, 1935. The time of operation as well as the patient must be carefully selected. The avoidance of anesthetic trauma is necessary to prevent reactivation of a quiescent pulmonary lesion.

When a diagnosis of unilateral destructive progressive renal tuberculosis is made, the treatment indicated is usually nephrectomy. The small destructive lesions of the ulcerative group may, with safety, be watched temporarily. Surgical treatment is indicated when pus cells and bacilli of tuberculosis are constantly present in the urine and the pyelogram reveals that the lesion is increasing. Repeated tests must reveal no lesion or bacilli in the urine obtained from the contra-lateral kidney before nephrectomy is attempted. The patient must have no other active local or general lesion of tuberculosis. With these

conditions present, the treatment of unilateral tuberculous parenchymal abscess and pyonephrosis is always nephrectomy.

In the presence of unilateral or bilateral non-destructive renal tuberculosis, surgical treatment is not indicated. The patient should receive constitutional treatment and the local and general condition should be frequently checked to reveal evidence of a destructive process. With the appearance on the pyelogram of evidence of some slight destruction nephrectomy should not be done immediately but the lesion should be watched for a time. A possible undiscovered lesion in the other kidney and the presence of much good functioning kidney tissue in the affected kidney may postpone nephrectomy until it is apparent that the lesion being watched will not be controlled. With proper constitutional treatment small lesions may be held in abeyance for a long time.

When the patient has bilateral destructive lesions of renal tuberculosis, constitutional therapy and heliotherapy become the first considerations. In the event that one kidney is destroyed and the other kidney shows evidence of good function, and the tuberculous lesion is non-destructive, nephrectomy may be indicated provided that the patient has shown a good resistance against other lesions of tuberculosis. Occasionally nephrectomy may be indicated or justified when a patient with bilateral destructive lesions of tuberculosis has severe pain, uncontrolled hemorrhage or obstruction of the ureter with pain and toxemia. The span of life, in the patient with bilateral destructive lesions, is governed by the amount of good functioning renal tissue that he possesses. In the presence of bilateral non-destructive renal tuberculosis the treatment is medical. About 65 per cent of the early lesions of renal tuberculosis are bilateral.

Nephrectomy in renal tuberculosis is practically never an emergency procedure. There is plenty of time for all factors to be considered before surgical treatment is attempted.

If a *perinephritic abscess*, whether tuberculous or non-tuberculous, should develop in association with unilateral or bilateral renal involvement, the treatment indicated is immediate surgical drainage. If the patient is in poor general condition, only drainage of the abscess should be done. With the complication of perinephritic abscess, nephrectomy should not be attempted since then it is a procedure attended by considerable extra risk. The kidney associated with a tuberculous perinephritic abscess may be completely destroyed and all renal tissue extruded through the drainage opening. The drainage of this purulent material may result in almost miraculous improvement in the condition of the patient.

Heliotherapy is indicated in all cases of extrapulmonary tuberculosis. The use of ultra-violet therapy is indicated only in certain instances. The beneficial effect of actinotherapy on tuberculous lesions, particularly extrapulmonary ones, has been known for a long time. However, at times it is used unwisely. We cannot be sure whether the beneficial effect of the ultraviolet therapy comes from a local antiseptic action of the actinic light or whether it is due to a stimulating action on granulating tissue by drying or heating. There can be no question that improved healing results in selected cases. Overdosage must be avoided. In a patient who has to travel some distance daily to receive treatment, better results may be obtained by keeping him or her at home with rest than with the use of actinic therapy.

Surgical patients should have very careful preoperative and post-operative treatment. When the usual careful diagnostic routine is followed, the patient will have had considerable constitutional treatment, rest and heliotherapy before operation. The recuperative powers of tuberculous patients are decreased; consequently a patient who submits to any surgical procedure should be required to remain in bed, at rest, with heliotherapy when possible, from one to six months following the surgical treat-

ment. This length of time required for bed rest can be decided when the resistance, temperature and general condition of the patient are known. *The treatment of renal tuberculosis should be directed at the patient as a whole and not alone at the local lesion.*

CONCLUSIONS

1. All patients with tuberculosis should have routine urinalyses every three months.

2. Patients showing cellular elements in the urine should have a complete urological study.

3. The destructive lesions of renal tuberculosis can be differentiated only by well-filled retrograde pyelograms.

4. The successful surgical treatment of urogenital tuberculosis depends primarily upon an accurate diagnosis. This may be accomplished only after repeated complete urological examinations.

5. There is an early or "invasion" stage of renal tuberculosis just as there is with any other type of this infection. This period may be symptomless but a careful search will reveal clinical findings that are sufficient for a diagnosis.

6. The diagnosis and early treatment of the early lesion of renal tuberculosis may prevent the development of renal phthisis.

7. Surgical treatment for any type of tuberculosis, except in an emergency, should not be undertaken until the patient has developed a sufficient defense mechanism.

8. The progress of lesions of tuberculosis may be slow.

9. The surgical treatment of urogenital tuberculosis is rarely an emergency.

10. Surgical or medical treatment of tuberculosis should aim at the patient as a whole, not alone at the local lesion.

11. Renal tuberculosis or other urogenital lesions are local manifestations of a constitutional disease.

12. Non-destructive renal tuberculosis, unilateral or bilateral, is a non-surgical condition and should be treated intensively by medical methods.

13. Bacilli of tuberculosis in one speciment of urine obtained from the kidney pelvis do not alone give an indication for nephrectomy.

14. In early renal tuberculosis, surgeons should be more conservative in advising the removal of a kidney which eliminates bacilli of tuberculosis unless the pyelogram reveals definite evidence of erosion and the urine from the second kidney is repeatedly negative when injected into animals.

15. Unilateral slightly destructive tuberculosis should be treated conservatively under careful observation. Nephrectomy is indicated only when progressive disease is present.

16. Extensive unilateral destructive lesions should be treated by surgical methods.

17. Bilateral destructive renal tuberculosis is not a surgical condition except to stop hemorrhage or to relieve pain and sepsis, the result of an obstructed ureter.

18. Tuberculous patients should have careful pre-operative treatment.

19. Heliotherapy is beneficial but ultraviolet light should be given only in selected instances.

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Nondescent of both testicles is usually associated with lack of development elsewhere in the genital tract.

. . . . . .

Prolapse of the urethra is seen in little girls and in aged women; very rarely at other periods of life.

. . . . . .

The phthalein test, originated in 1910 by Rountree and Geraghty of Johns Hopkins University, . . . is elaborated in the bases that this drug is eliminated almost wholly by the kidneys; that the normal kidney will excrete from 60 to 85 per cent of the entire amount within two hours, and that its appearance in the urine takes place very soon after its injection into the circulation or the muscles.

From—"Urology for Nurses" by Oswald S. Lowsley, M.D. and Thomas J. Kirwin, M.D.

DIAGNOSIS AND TREATMENT OF MOVABLE KIDNEY

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THE importance of this subject is quite apparent when it is remembered that 20 per cent of all women and from 1 to 2 per cent of men suffer to a variable degree from movable kidney. In women the right kidney alone is movable in about 70 per cent, the left in 10 per cent, and both in 20 per cent. In men, however, the left kidney is almost as frequently involved as the right. The condition occurs independently of visceroptosis in over 90 per cent of cases. The incidence of symptom producing renal ptosis in women is 20 per cent, while in men there are very few cases of ptosis which are free from symptoms.

The problem has been, is now, and will continue to be one which will demand the most intelligent handling, with a very definite number of unsatisfactory results. There have been many rules established for the handling of this condition, with particular emphasis on certain phases, but few have treated the problem comprehensively.

Before the advent of modern urology, which dates from the advent of cystoscopy and urography, most valuable means of recognition of various degrees of ptosis were developed. Dietl, whose name has perhaps been the one most frequently associated with ptosis, has probably been as frequently misquoted and misinterpreted as any individual in medicine. The term Dietl's crisis, which Dietl himself never described as such, has been applied through the years to almost any type of discomfort in the region of either kidney in which any degree of ptosis could be demonstrated. This is far from what Dietl characterized in his original contribution in 1864 as incarceration or strangulation. In that contribution he described a condition consisting of acute obstruction to emptying of the renal pelvis accompanied by very severe reflex gastrointestinal symptoms, associated with fever of relatively long duration (that is, longer than a few hours or a day), and calling for very careful nursing, medication, and supportive treatment.

The symptoms directly attributable to renal ptosis are due to interferences with a satisfactory relationship between the renal pelvis and ureter with resulting obstruction, or to actual pulling and torsion on the renal pedicle itself. A ptosed kidney which does not cause one of these two effects will be most unlikely to produce any symptoms or call for any form of treatment.

The degree of ptosis has been arbitrarily defined by classing those kidneys which can be slightly palpated below the costal margin as of the *first degree*, those in which the upper pole can be palpated below the costal margin as *second degree*, and those which are lower than these as *third degree*.

In some instances the kidney may be so freely movable as to become an abdominal organ provided with a mesentery of its own.

The symptoms produced may vary from a simple dragging feeling in the lumbar regions, becoming progressively more pronounced as the day wears on, with relief upon retiring at night, to the sudden acute, sharp, stabbing pain in the region of the kidney, accompanied by nausea, vomiting, and shock of various degrees. In addition to these simple mechanical symptoms there are the symptoms incident to infections which develop and become superimposed in individuals with poor drainage. There is also a group of individuals who experience acute pain incident to physical violence. This question of importance from a medico-legal standpoint. In certain individuals the abdominal picture may be such that

intestinal obstruction and visceral pathology of various kinds might be confused with the condition.

From a physical diagnostic standpoint the contribution of Dietl is so excellent that a translation of it is presented as follows:

"The recognition of a movable kidney is generally attended with no particular difficulties. The fact that movable kidneys usually are associated with thin flabby abdominal walls and that the right is far oftener affected by prolapse than the left kidney facilitates the examination and affords it a certain point of support.

"If the occasionally constipated bowels have previously been thoroughly evacuated by a purgative or an enema, as a rule palpation and percussion suffice to establish the diagnosis. We feel close to the border of the liver, more rarely deep below the same in the direction of the umbilicus, a longitudinal, almost rectangular, hard, smooth, sensitive, extremely movable tumor, which evades every moderately firm and suddenly applied pressure of the fingers, so that it can again be located not without care. The tumor thus demonstrated may be removed from the vicinity of the liver by staccato pressure and displaced slightly downward (or to one side), but even more readily brought down below the right costal arch, where it immediately disappears. By powerful pressure with the palm of the hand applied to the right lumbar region the tumor may be pushed forward towards the abdominal region and, vice versa, by means of pressure on the latter, backward into the lumbar region, so that it is rocked back and forth simultaneously between the palms of both hands, especially when the patient is in the sitting position. The tumor rises during deep inspiration, because the kidney has become displaceable and must yield to pressure of the diaphragm upon the liver and intestines. Percussion over the tumor is always tympanitic provided the bowels have been properly evacuated. If the tumor is removed from the border of the liver, the tympanitic intestinal sound presents the delimitation of the same from the hollow hepatic sound. If the patient is made to assume an elbow-knee position, the right lumbar region appears flat (shallow), even sunken, and the percussion sound over the same is clearer than on the left side, while the sunken kidney is distinctly palpable against the abdominal wall. These physical signs are, aside from the characteristic functional disturbances, which are common to other similar tumors, such as liver, gallbladder, fecal, and retroperitoneal tumors, quite sufficient to establish the diagnosis of a movable kidney, even though the latter should appear with symptoms of irritation and incarceration."

In addition to these physical signs there are available urinalysis, cystoscopy, and urography. It is not uncommon to find albumen in urine from a patient with ptosis. Upon cystoscopy in individuals where ptosis is producing symptoms, the ureteral meatus on the side involved will not spurt as freely as on the uninvolved side. Upon ureteral catheterization and aspiration, where the ptosis has produced hydronephrosis to any degree, more than the usual normal 20 c.c. of urine will be aspirated, and the renal function as indicated by the phenolsulphonephthalein method will be relatively less than the normal.

With the usual method of single pyeloureterogram the degree of ptosis where no hydronephrosis exists may not be evident. In order to demonstrate ptosis urographically one of the following methods should be used: (1) Urograms must be taken in the prone and upright position. (2) Serial urograms with different phases of respiration from that of complete expiration to extreme inspiration. It is not an uncommon experience to see as many as three or four urograms which fail to demonstrate the extent of the condition along with only one which does demonstrate it. (3) The method of serial pyelography practiced by Moore is perhaps the most practical because it can be done with least difficulty. (4) The method of Jarre and Cumming is very valu-

able but has not been widely used because of the lack of availability of the complicated mechanism necessary for its employment. (5) The best method is direct fluoroscopy using skiodan with retrograde ureteral catheter injection, with the patient in both the prone and upright positions. Unfortunately this method has not become popular owing to the time consumption and coordination of personnel required for its use. (6) The ideal method would, of course, be motion picture film records of the fluoroscopic visualization of the upper urinary tract following the intravenous administration of some compound which would be excreted in sufficient concentration to render fluoroscopic visualization satisfactory. William Stewart of New York has already successfully produced motion picture records of the urinary tract. At the moment there are so many technical difficulties that this method is not feasible, but with the rapidity of improvement in this highly technical field it is not unreasonable to look forward to the time when such a method of examination will be entirely practicable.

Interferences with the satisfactory relationship between the renal pelvis and ureter are easily recognized by either the serial or fluoroscopic method of examination. Torsion and rotation are demonstrated. The varying degrees of hydronephrosis when present are readily perceived. The various pain-producing abnormal neuromuscular mechanisms characterized by localized spasm in any portion of the renal calyces, pelvis, or ureter may be recognized. This particular group of pain producing motility syndromes should always be borne in mind because of the fact that they alone are the pain producing agent in some instances and may respond to simple medication. It should be remembered that these syndromes are not necessarily caused by the ptosis and occur in normally placed kidneys.

Before going on to the treatment of this condition, one point cannot be emphasized too strongly, namely, that all sorts of functional disturbances producing either abdominal or other symptoms, without the demonstration of very definite obstructive mechanism or neuromuscular dysfunction due to renal ptosis, should by no means be subjected to nephropexy.

The treatment of ptosis of the kidney presents many individual problems and has passed through eras of enthusiasm and pessimism so far as nephropexy is concerned. The eras of enthusiasm have been due to exaggerated reports of favorable results of nephropexy and the widening of the indication for operation in all types of neurasthenic and functional nervous disturbances which make up an entirely different problem group. The eras of pessimism have ensued in consequence of the unfavorable results which are bound to occur when operation is carried out in this large group of individuals who have functional nervous disturbances and such symptoms as constipation, nausea, lassitude, et cetera. At this point it should be made clear that properly performed nephropexy in properly selected individuals is productive of as large a proportion of not only satisfactory but brilliant results as any surgical procedure.

All things being equal, the individual with marked ptosis of the third degree with severe symptomatology will be most likely not to respond to belts or increase in weight, therefore nephropexy should be performed. The operation of nephropexy should observe the following principles: (1) The kidney and upper ureter should be very completely mobilized so that regardless of the position in which the kidney may be fixed, the relationship of the upper ureter and pelvis may allow of proper accommodation. (2) In view of the fact that pain production may be prevented by interference with the nerve supply to the kidney, stripping of the nerves from the renal pedicle should be done. In addition to this, by stripping the nerves from the renal pedicle most of the pain-producing abnormal motility syndromes which may or may not have been recognized will be remedied. In the detailed technique of this

neurectomy, it should be emphasized that every tiny nerve fiber is not searched for with a magnifying glass around the renal vein and artery as once described, but that it should consist of severing the main nerve or group of nerves where they first start to divide and follow along the renal vein and most frequently the renal artery. When these groups of nerves are severed and the renal pedicle is completely mobilized and conservatively stripped, the technique of the neurectomy has been carried out to a sufficient extent. (3) The bed in which the kidney is to lie should be well cleared of fat so that satisfactory adhesions may readily form. While it has been stated that no fixation is necessary in order to have the kidney adhere in a proper position, it does not seem reasonable to omit some simple form of fixation when it can be so easily accomplished. All things being equal, the simpler the method of fixation the better. Above all, no mechanical arrangement in the way of building up supports beneath the renal pelvis should be attempted, because of the possibility of the development of tissue bridges which may in themselves produce actual obstruction. The simplest form of fixation is the use of one suture introduced about two-thirds the way up the lateral border of the kidney approximately 1½ centimeters to one side of the midline, and running downward beneath the capsule to the most dependent point of the inferior pole, across the inferior pole, and up the other side. The two free ends are then run through the posterolateral abdominal wall just beneath the last rib, and pulled up so that the inferior pole is lateral, thereby affording the pelvis the best possible position for emptying. One very important precaution and principle in this fixation is not to attempt to fix a kidney so high that a low lying liver will probably push it down gradually and cause it to give more trouble subsequently. The height at which the kidney is fixed is not at all important. The main factor is that it be fixed in a position where the renal pelvis may accommodate itself satisfactorily to the upper ureter and where the various forces will have the least possible chance of pushing it downward and again disturbing the uretero-pelvic relationship.

The treatment of ptosis of the second degree is more variable. If the individual is thin, and it appears that the use of an abdominal belt with kidney pad and the putting on of weight offer some chance of remedying the symptomatology, these measures should by all means be tried before recourse to operation. When these expedients fail, or when definite hydronephrosis has developed, nephropexy should be performed.

In the first degree of ptosis much patience should be displayed in attempting to relieve the complaint by the putting on of weight, abdominal pads, and the use of the various drugs which control neuromuscular dysfunction, such as eserin, the barbiturates, calcium, belladonna and its derivatives, and ephedrin, and if any endocrine dysfunction is apparent, attempts to remedy this. Ureteral dilatation will occasionally relieve symptoms, but usually calls for repeated dilatation and not infrequently wears out the individual's patience so that he or she prefers surgical relief. In individuals who will not respond to conservative treatment or who have developed hydronephrosis, nephropexy is the procedure of choice.

In conclusion, the handling of patients with symptom-producing nephroptosis of various degrees should constitute a very satisfactory phase of urology when such a high percentage of successful results may be obtained with patient and intelligent investigation and treatment.

END-RESULTS OF PLASTIC OPERATIONS ON THE KIDNEY PELVIS FOR HYDRONEPHROSIS

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FROM the early days of kidney surgery, there has been dissatisfaction among surgeons with nephrectomy as the invariable treatment of hydronephrosis. It, of course, relieved the symptoms, but frequently at the expense of functioning kidney tissue. When the opposite kidney was normal, this was of little consequence, but when the other kidney was absent or markedly diseased, it was disastrous.

So it is not surprising that quite early in the modern era attempts were made to devise plastic operations which would give an alternative to nephrectomy or permanent nephrostomy.

The first attempt of this kind was by Trendelenburg in 1886, but it remained for Kuster, in 1891, to demonstrate that such operations could be successful, and he made the prediction that in time such operations would become the usual and accepted method of treatment for hydronephrosis. His success encouraged others to similar efforts, chief among them being Israel, Albarran, Riedel and Kümmell.

In 1908, Kroiss was able to find in the literature 102 instances of plastic operations on the pelvis, of which seventy were considered successful by the standards of the time, and three years later Weinberg collected forty nine additional cases.

During the next decade, in spite of the fact that there were reports of such operations from the clinics of Wildboltz, Gregoire, Simon, Goebell, Kroiss, Oehler, Gayet, Meyer, Schloffer, Zimmerman, Habler, and Mayo, this type of operation fell more or less into abeyance. The war may have had something to do with this. Be that as it may, in 1922 Frank and Glas, in reviewing the discussion of hydronephrosis which took place at the German Urological Congress in Vienna in 1921, declared that up to that day nephrectomy was everywhere the standard operation for hydronephrosis.

About this time a new interest became manifest in hydronephrosis, its causes and treatment, and a new group of surgeons directed their interest toward the conservative treatment of hydronephrosis. This interest has persisted and has gradually widened.

In recent years there have been reports by Bailey, Bazy, Boerminghaus, Braasch, Cabot, Creevy, Eisendrath, Ferria, Foley, Frontz, Harris, Heckenbach, Henline, Hinman, Hryntschak, Krogius, Lubash, Mathe, Moore, Ormond, Papin, Peck, Priestly, Quinby, Roch, Sargent, Schaffhauser, Scholl, G. G. Smith, von Lichtenburg, Walters, Wildboltz, and Young.

Some of these have reported surprisingly large series of cases. Nevertheless, it remains true today, as it was fifteen years ago, that most hydronephrosis requiring operation, including such cases as might be considered fit subjects for plastic surgery, are treated by nephrectomy.

This fact argues for unfamiliarity on the part of the profession in general with the methods which can be employed; for the lack of confidence in plastic operations as a remedy for hydronephrosis; or possibly for a lack of agreement as to the preferable type of operation and lack of standardization of procedure. Moreover, it is objected that in some cases reported as successful, the evidence of success is inconclusive, and there seems to be an impression current

that many cases at first apparently successful later come to grief through infection or trauma.

Therefore a review of the methods used, and a survey of end-results is timely. This should show what measure, and what proportion of success is possible; whether such success is permanent; what types of operation offer the best chance of success; what preoperative and post-operative measures are advisable or indispensable; and what adjuvant procedures are useful.

All plastic operations are of course based on the common sense theory that most hydronephrosis is due to mechanical obstruction, removal of which should remedy the condition to the extent of checking its progress and permitting as much restoration as is possible. There are undoubtedly cases of neurogenic dysfunction of the pelvis and ureter causing hydronephrosis, but they are the exception, and in the vast majority of cases of hydronephrosis, a mechanical obstruction can be demonstrated.

There are only four types of obstruction pertinent to this discussion. They are:

1. Compression or kink at uretero-pelvic juncture caused by bands, either fibrous or vascular.

2. Stricture of the uretero-pelvic junction.

3. Kinking of ureter at the pelvis caused by ptosis or adhesions either inflammatory or congenital, and

4. Valve formation caused by high insertion of the ureter into the pelvis. This condition is caused by enlargement of the pelvis and itself becomes an obstructing factor and a cause of further pelvic enlargement.

We are not concerned with obstruction of the ureter proper, nor with calculous obstruction, though in any particular case of the latter, it cannot be taken for granted that the stone is the sole cause of obstruction, for on the one hand, the role of obstruction in the causation of stone is well known, and on the other, a stricture at the uretero-pelvic juncture may prevent the passage of a stone, which otherwise would have passed easily.

Conservative operations designed to remedy hydronephrosis are of two kinds:

1. Those which do not involve incision into the pelvis or ureter, and

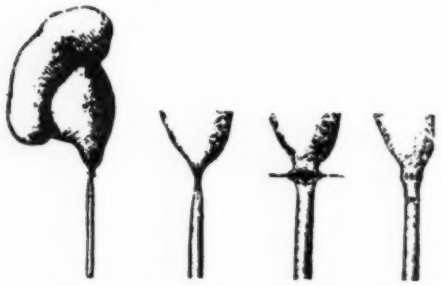
2. The true plastics.

Those which do not involve incision into the urinary passages are those in which the only procedures are some form of fixation of the kidney, or the sectioning of a fibrous or vascular band.

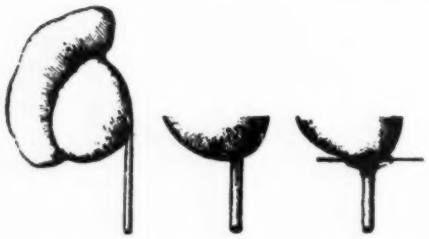
Nephropexy needs no prolonged discussion. Much has been written about it, and several methods have been devised. After falling into disrepute for many years due to its indiscriminate use, it has gradually been reestablished as a useful procedure in a limited class of cases, with very definite indications for its employment.

Hydronephrosis may be caused by bands—either fibrous or vascular—which constrict, compress, or kink the ureter or the uretero-pelvic juncture. Fibrous bands may of course be sectioned freely. The vascular bands are the more common and such a band may contain an artery or a vein or both. Veins may be sectioned freely, but some years ago Hinman and Hepler published some work showing that such aberrant arteries were usually end arteries and that their section would cause infarction of a portion of the kidney, which if the vessel were large and supplied a large portion of the kidney, would be undesirable and might be disastrous. Some recent work goes to show that these are not invariably end arteries, but extensive necrosis, sometimes leading to secondary nephrectomy following section of such arteries has been reported (Christensen, Belt, Ball-Guling, Frank and Glas, Granhahn, Lassio, Essendrath and Wolfram). Heckenback reports a septic icterus resulting from an infected infarct, and Marion a temporary renal fistula due to partial renal necrosis. Wildboltz observed long continued albuminuria and Young reported important reduction in function.

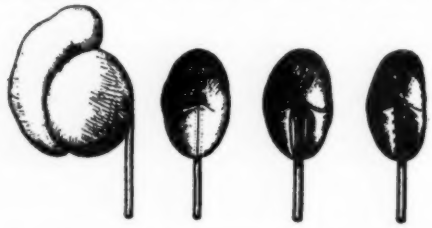
To prevent such mishaps, attempts have been made to loosen compressing vascular bands by high nephropexy. Failures often resulted and in some instances nephrectomy later became necessary (Hutchinson, Wildboltz) because the vascular band tightened again. Moreover, cases are on record in which bands have been resected and a stricture of the ureter overlooked (Andler, Lequeu, Nevers). Some of the true plastics have been devised to obviate the necessity of sectioning vascular bands, the ureter



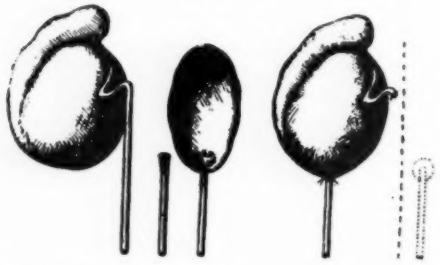
(After Oehlicher.) Fenger's Operation for Stricture



(After Oehlicher.) Fenger's Operation on Valve

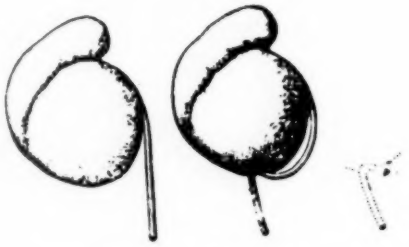


(After Oehlicher.) Trendelenburg's Intra-pelvic Operation on Valve

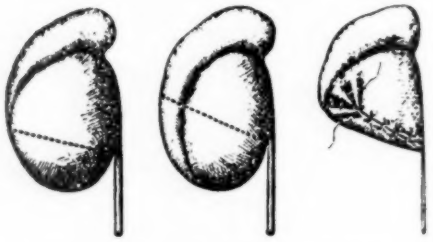


(After Oehlicher.) Kuster's Ureto-pyelo-neostomy. Delfet

(After Schwyzer.) Schwyzer's Method

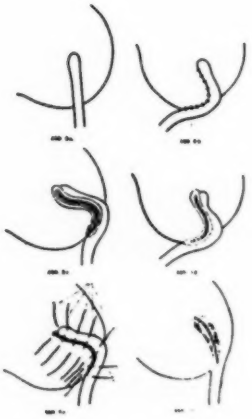


(After Oehlicher). Albarran's Lateral Anastomosis



(After Oehlicher.) Pelvic Resection. Albarran's Orthopedic Resection. Israel's Plication

(After Oehlicher.) Nephropexy after Plastic. Methods of Drainage and Splinting, after Plastics



(After von Lichtenberg.) Von Lichtenberg's Method

being sectioned instead, and reimplanted into the pelvis on the other side of the band.

The true plastic operations can be divided into four types: the Fenger (Heinecke-Mikulicz) operation; ureteropyeloplasty; reimplantation of the ureter into the most dependent portion of the pelvis; and resection and plication.

The Fenger operation is like the Heinecke-Mikulicz operation on the pylorus and consists in incising a stricture and suturing in the reverse direction.

Several kinds of ureteropyeloplasties have been devised, the best known being those of Albarran, von Lichtenburg, Schwyzzer, and Foley. Albarran's operation consists in a lateral anastomosis between pelvis and ureter. Von Lichtenburg's operation resembles the Finney pyloroplasty, Schwyzzer's original operation consisted in a Y incision—the V being in the pelvis and the stem down the ureter. The V flap is brought down to the lower end of the stem and sutured there, thus widening the uretero-pelvic juncture.

Foley's operation is a modification and improvement of Schwyzzer's. He has moved the longitudinal incision of the ureter to its lateral aspect, that is, to the surface next the kidney, and extended the V incision, one arm to the anterior and one to the posterior aspect of the pelvis, so that the sutures bring the opening of the ureter to a more dependent position. This operation is now known as the Foley Y plastic.

Reimplantation of the ureter may be done in three ways: in one a small collar of pelvic wall is excised with the ureter and reimplanted into the pelvis; in the other two, the ureter is sectioned and reimplanted into the pelvis, either suturing the pelvic wall around it like a cuff, or suturing the cut edges in accurate apposition.

Resection and plication require no explanation.

Conservative treatment of hydronephrosis is imperative when there is a solitary kidney or both kidneys are hydronephrotic. Here plastic surgery may be the only alternative to permanent nephrostomy and the surgeon must know what plastic operation offers the best chance of success. Conservatism is optional when one kidney is normal; and in this case the surgeon wishes to know not only which is the easiest and most promising, but whether, taking everything into consideration, the attempt is worthwhile.

The ultimate criteria of the success of plastic operations for hydronephrosis are relief of symptoms and conservation or restoration of function. Elimination of infection and anatomic restoration are desirable but not essential.

In the earlier days function tests were not possible—nor were pyelograms. Later, function tests were devised and pyelography came into use, but required cystoscopy which made it a disagreeable and cumbersome procedure. Now however, in intravenous urography, we have a simple and convenient method of measuring both functional and anatomical restoration. Clinical relief of symptoms in the presence of a normal kidney on the other side is not sufficient ground for claiming success—for as Cumming pointed out recently, renal atrophy sometimes takes place in such cases, and the symptomatic relief may be accompanied by destruction of the kidney just as complete as if nephrectomy had been performed.

Only through a consideration of a large number of cases, especially of those which have been observed over a long time, can we draw conclusions regarding the possibility of success, the suitability of operations, and regarding the validity of objections which have been raised.

In the literature there are recorded a few isolated cases which have been demonstrated by autopsy, or otherwise, to be successful many years after operation. Bazy demonstrated a kidney with good drainage and good parenchyma twenty-four years after uretero-pyelo-neostomy. Hartman had a good result from a Fenger operation after twenty one years. Legueu, fifteen years after uretero-pelvic anastomosis found the kidney functioning and drain-

ing well. Wildboltz used Kuster's operation on a large infected traumatic hydronephrosis and twenty years later it still showed some function, and in the meantime had been symptom free. In another instance he performed a Fenger operation on a hydronephrosis the size of a child's head, and found sixteen years later, that there was only slightly less function on this side than on the other. In two other cases there were good results sixteen years after pyeloneostomy. Von Lichtenburg, sixteen years after pyelo-uretero-neostomy, removed the kidney for carbuncle and found it functioning. He also had another case in which the other kidney was removed sixteen years later, and the patient survived.

These isolated reports surely prove that permanent success of plastic operations is possible, but indicate nothing as to the frequency of success. A review of the results obtained in a long series of such attempts by many different operations is necessary to the appraisal of the chances of success, the determination of the indications and contra-indications for operation, and for decision as to the best methods of operation.

The longest series is reported from the Mayo Clinic. Walters, Cabot, and Priestly report seventy-one plastic operations in sixty four patients, with fifteen secondary nephrectomies and two deaths. All these were done in the past few years, and in 89 per cent there were satisfactory follow-up reports. They regard 70 per cent of their results as at least satisfactory, and report diminution in the size of the pelvis in a large portion of their patients. They favor resection of the pelvis and reimplantation of the ureter into the portion of the pelvis remaining, though they have used other methods. They have used the splinting catheter and nephropexy in most instances.

From the clinic of von Lichtenberg and Heckenbach, sixty nine conservative operations for hydronephrosis are reported, with fifty two successes, at the end of a year and a half. There was one death. These figures, however, require modification, for many of their conservative operations were not plastic operations on the pelvis in the sense used here. On scrutiny we find twenty two true plastics, the other operations being heminephrectomy, resection of vessels, dilatations of the ureter, etc. Von Lichtenberg recommends excision of the twelfth rib for exposure, if necessary, and has chiefly favored the uretero-pyeloplasty known by his name, or resection of the pelvis with reimplantation of the ureter into the remaining portion, suturing the pelvic wall about the ureter like a cuff.

Wildboltz reports fourteen plastic operations, with one failure. His observations cover many years and include reimplantations, uretero-pyeloplastics and Fenger operations. He favors preliminary nephrostomy in the presence of infection.

Quinby in 1929 had sixteen cases, of which two were unsuccessful. Most of these were ureteral reimplantation about a vascular band. Two were Fenger operations—both failures. His cases have been observed over many years and show satisfactory results. He does not use a splinting catheter, sutures the ureter to the pelvis with accurate apposition of the edges and advises that infection be treated before operation.

Foley reports twenty one Y plastic operations on nineteen patients with no failures and two deaths. All of his operations must have been in cases of stricture of the uretero-pelvic juncture, or of high implantation of the ureter. He uses nephropexy when indicated and closes his ureteral and pelvic incision with a large number of fine cat gut sutures placed close together. He has followed some of his patients for ten years.

Creevy reports ten cases; nine Y plastics with one failure requiring nephrectomy, and one successful case of section and reimplantation of the ureter. His observations are all of comparatively short duration. He has noted diminution in the size of the pelvis and clearing of infection, favors a splinting catheter and catheter drainage of the pelvis.

Sargent reports twelve cases with one poor result in a Y plastic. He has used the Fenger operation three times. He emphasizes the possibility of anatomic restoration.

T. D. Moore has twelve cases observed over several years with two unsatisfactory results.

Hryntschak, in 1936, reported thirteen cases with two unsatisfactory results. Most of his patients had been observed less than four years. He lays stress on adherence to the general principles of all plastic surgery as essential to success.

To sum up then, we have here reports of one hundred and ninety-one cases with a high rate of success. Of the 169 cases in which there is definite information, there were only four deaths and twenty-five failures, a death rate of 2.3 plus per cent, and a failure rate of 14.8 minus per cent.

In addition to these longer series are some shorter series in which the results varied a good deal.

G. G. Smith, in 1931, reported six cases with one secondary nephrectomy and one questionable result.

Henline, in 1935, reported on seven cases with two failures and one death from thyroid crisis. Most of the operations reported by him were of the Fenger type, and most of them had been observed for only a short time.

Patch has reported a short series in which he implanted the ureter with a collar of pelvic tissue, and regards his results as satisfactory.

Kimbrough, in 1935, described six cases, all successful, though most of them were observed for only a short time. He used the splinting catheter.

Schaffhauser, in 1936, reported five cases observed less than four years—all satisfactory. He most often used the Fenger operation. He believes infection is a contraindication to operation.

In 1936, I reported five failures, two of which were converted into successes by second operations; two of which required secondary nephrectomy; and one of which continued to have symptoms. Since then, one patient who had been symptom free for seven years has returned with recurrence of symptoms, similar to those of which he originally complained, but which have not yet been investigated.

Scattered through the literature, in discussions, etc., are references and allusions to isolated cases and short series with varying success. In this country Morrissey and Randall speak unfavorably of the operation—as do Marion, Cifuentes and Allesandri in Europe.

SUMMARY AND COMMENT

It is evident that not only is it possible for plastic operations to be successful, but that success has actually attended by far the greater number of such operations performed by the group of surgeons who have the most experience with this type of surgery. This has not been true to the same extent of the occasional operator.

When failures occur, they are recognizable early, usually immediately and certainly within a year, with rare exceptions. I have had one apparent recurrence after seven years, and Quinby reports one after a similar period, but they are the exceptions.

The danger to life is not great. It is safer than nephrectomy. Heckenbach reports from Von Lichtenburg's clinic a series of forty-six nephrectomies for hydronephrosis with one death. In the series cited earlier, there were only four deaths in 174 operations.

Infection as an obstacle to plastic surgery has been overemphasized. It must be respected and treated both before and after operation, often by preliminary nephrostomy and always by post-operative drainage, but instances of healing in spite of continuing infection, and failure to remedy obstruction are on record. I have one such case. Deep seated infections of long standing may persist along with relief of symptoms and improvement in function.

In successful cases there will be relief of symptoms, some functional restoration,

and there may be considerable anatomic restoration.

Interruption of the nerve and blood supply by section of the ureter seems of little consequence. Those who have practiced section of the ureter with reimplantation, have had no more failures than those who preferred uretero-pyeloplasty.

The evidence seems to be hostile to the theory of renal counterbalance, unless it may be construed as evidence in its favor that solitary kidney or bilateral hydronephrosis seem to offer the most favorable opportunity for successful plastic operation.

There is difference of opinion as to the value of resection or plication of the pelvis. On one hand, it is argued that no resection or plication can restore power to an overstretched and atrophied pelvic muscle; on the other hand, it is admitted that either procedure will diminish the residual reservoir, which may be worthwhile. On the whole, the evidence seems to favor resection, even though it adds to the length of operation and to the amount of manipulation involved. I have tried it just once, in a case in which the ensuing failure could not be blamed on this procedure.

The balance of opinion and the evidence is rather strongly against the Fenger operation. It is a seductive procedure—it looks simple, but in reality it requires finer judgment than the other operations. If the incision through the stricture is a shade too long, or if the stricture is long, suturing in the reverse direction may cause puckering and a reformation of the obstruction it set out to remedy. It seems to have been a favorite with those who have undertaken plastic operations only once or twice and this may explain their discouragement with plastic surgery. Nevertheless, there are those who feel that this operation has a place, and who have used it with satisfaction. Two of my failures were with this type of operation.

The operations of ureteral reimplantation and uretero-pyeloplasty seem equally successful in the hands of those who use them. My own preference is for reimplantation, for it does not necessitate the section of a vascular band, and is as applicable to stricture and high ureteral implantation as is uretero-pyeloplasty. It seems to me simpler; to require less manipulation; and to make less demand on the judgment. This however, is only a personal opinion, and certainly the results obtained by Foley and Creevy speak for themselves.

Three methods of reimplantation have been mentioned: one in which a small collar of pelvic tissue is excised with the ureter and reimplanted into the pelvis; the second in which the ureter is allowed to project into the pelvis for a short distance, the pelvic wall being sutured about it like a cuff; and the third in which the ureter is sutured to the pelvic opening with accurate apposition of the cut edges. The evidence of their value is conflicting, and it is possible to give only a personal preference. I prefer the third. It seems to me that it would be possible to overlook a stricture or valve at the juncture, in the first method, and that it would be possible to create a valve by the second. This latter has been reported. However, von Lichtenburg has used the second method with satisfaction and it is possible that Lubash's recently described method may eliminate danger of valve formation. I have had two failures using the second method, remedied later by reoperation with suture in accurate apposition. This successful result, however, may have been due to the long continued splinting of the ureter.

There are three subsidiary procedures concerning the use of which there is little difference of opinion. Nephropexy is favored by most surgeons whenever indicated; post-operative pelvic drainage is favored by nearly all operators; and the use of the splinting catheter in the ureter is almost universal. Quinby argues against it, and his record of success gives his opposition great weight, but the balance of opinion is against him. In this connection, a very striking case is reported by McArthur, in which a hiatus in the ureter

was bridged around a splinting catheter which was left in place for a long time, with complete restoration of the ureter.

CONCLUSIONS

In arriving at final conclusions, all the above facts, opinions, and arguments must be considered, and in addition due weight must be given to the following: the special importance of conservation of renal function in certain classes of patients—particularly in young women in the child bearing age; the fact that with one good kidney, the importance of the other varies inversely with the age or directly with the life expectancy; and the factor of expense and loss of time.

Giving all of these their proper weight, it seems to me that the following final conclusions are justified:

1. With the solitary kidney or with bilateral involvement, conservatism is mandatory and plastic surgery should be employed. Resort can be had to permanent nephrostomy if this fails.
2. In the presence of one good kidney (and this should not be considered good unless the pyelogram is normal, the function excellent, and no infection is present) if in the involved kidney there is function worth preserving:
   - *A.* Plastic surgery is indicated in children and young adults, especially in young women in the child-bearing age.
   - *B.* Nephrectomy is the preferable procedure after the age of 50.
   - *C.* In the middle years, decision should be based primarily on the experience of the surgeon in this type of surgery; and secondarily, on the financial status of the patient; for failure means increased expense and a lengthened period of disability—matters of serious import to the vast majority of patients.
3. If plastic surgery is decided on, one of the proven methods of ureteropyeloplasty, or section and reimplantation, should be chosen, rather than the Fenger operation.

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In 1879 Neisser discovered the gonococcus. Nitze introduced cystoscopy. In 1881 Hahn performed nephropexy. In 1905 Schaudinn discovered the parasite of syphilis.

From—Garrison's "History of Medicine."

RADIATION TREATMENT OF THE MORE COMMON KIDNEY TUMOR*

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THE purpose of this paper is to discuss the management of Wilms' adenomyosarcomas, adenocarcinomas of the renal parenchyma in adults, and papillomas and epidermoid carcinomas of the kidney pelvis.

Although surgery is the principal agent in the treatment of most kidney tumors, the technique of different operations and the indications for their use are common urological knowledge and need not be repeated here. Irradiation of renal tumors, on the other hand, is still in an early stage. No adequate series of cases exists from which one can even approximate the end-results of its use. However, when radiation has been applied to the more common types of kidney tumors with all factors checked as carefully as clinical experiments permit, there has been sufficient regularity in their response to indicate in a general way the advantages and limitations of the agent.

The most practical radiation for the treatment of all renal tumors is furnished by the 200 kilovolt Roentgen ray unit. Super-voltage units, such as the 1,000 kilovolt machines, are somewhat more efficient in treating deeply situated tumors, but they are not in general use at present.

If the urologist chooses to employ radiation he must make as accurate a diagnosis as present methods permit, because the management of each patient must be planned in advance. Each type of kidney tumor is a separate disease entity with its own natural history and radiosensitivity. Unfortunately there are at present no procedures short of incising the tumor which are sufficiently refined to give such an exact differentiation. Furthermore, irradiation technique has not advanced to the point where the fullest advantage could be taken of such complete information. Hopes were high that aspiration biopsies would disclose histological make up of kidney tumors and that appropriate treatment could be based on these findings for each patient, but such is not the case. The technique of aspiration biopsy is not difficult and when properly performed the method seems to have little danger. It is of great diagnostic value in certain cases, especially in differentiating tumors from cysts. Trained pathologists can recognize characteristic cells in aspirated material and state with assurance that a tumor is present but the specimens are inadequate to disclose the type of tumor or its radiosensitivity.

Present diagnostic methods enable one to determine in most cases whether the tumor is primary or secondary in the kidney, whether or not the renal growth is operable, and whether or not metastasis has occurred. This information, together with an accurate estimate of the patient's general condition and the function of the opposite kidney, is fundamentally important in all cases because it furnishes the basis upon which the choice of therapy rests.

The older writers emphasized the care required in differentiating primary renal tumors, from metastases in the kidney, from primary foci elsewhere. Although the subject seems to have been ignored in more recent years, its importance was demonstrated when the first fifty cases referred to the registry of the American Urological Association were examined and 10 per cent were found to be secondary deposits rather than primary tumors.

WILMS' ADENOMYOSARCOMAS

In the great majority of cases, when a Wilms' tumor has been discovered the

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disease is far advanced. Therefore no time should be lost in establishing the diagnosis if the condition is suspected. An infant was recently referred to the writer with a note stating that two physicians had been unable to decide during the preceding nine months whether a growing mass in the left abdomen was a kidney or the spleen. In fifteen minutes an excretory pyelogram clearly showed a Wilms' tumor. It should be common knowledge that no matter how young an infant of either sex may be, a complete urological examination can be performed without harm, and that delay in diagnosis may destroy the child's chance of recovery.

Principally because they are made up of embryonal tissues Wilms' tumors grow so rapidly and spread so early that surgery alone has practically no benefits to offer. While it is true that radiation has not yet cured many patients, it is only because the disease is rare and much of the irradiation has been inadequate. At any rate, since the advent of radiation a surgeon need not attempt the removal of a tumor weighing 25 per cent or more of the infant's body weight, and for the same reason the more hazardous transperitoneal approach to the kidney can be abandoned.

Radiation should play a prominent part in the treatment of every Wilms' tumor. If the minimal dose of radiation necessary to control Wilms' tumors were known, and if it had been proved that this amount of radiation could be delivered to the kidney region of a child with no serious deleterious effects in later years, the writer would unhesitatingly prescribe radiation alone for every case. In the few personal cases in which full doses of radiation have been given and no surgery has been employed, the results within two years have been as good as or better than when a short pre-operative cycle has been followed by nephrectomy: as yet no ill effects of radiation have been noted. However, only a larger number of cases observed for several years will furnish data upon which definite opinions can be based. It may be that nephrectomy has been performed so soon after irradiation that sufficient time is not permitted for the series of changes which end in devitalization of tumor cells to take place. Since the importance of this point has been strikingly demonstrated experimentally with transplantable tumors, it might be well to follow the lead clinically when treating Wilms' tumors. At present, radiation alone is recommended in all cases in which the disease has spread beyond the kidney either by local extension or more distant metastases, and radiation followed by nephrectomy and post-operative irradiation when the tumor is limited to the kidney.

Pre-operative irradiation is given with the purpose of reducing the size of the tumor and facilitating nephrectomy. While destruction of tumor tissue is marked, no effort is made to accomplish complete sterilization of the growth.

Satisfactory irradiation may be given with the 200 kilovolt Roentgen ray unit using a target skin distance of 50 centimeters, filtration of ½ millimeter of copper and 1 millimeter of aluminum, and three skin portals, anterior, posterior, and lateral centering at the tumor. Portals in children with Wilms' tumors are usually about 9 by 6 centimeters. If the patient is not too young or too weak 200r can be given to a single portal daily—otherwise a smaller dose is better. If well tolerated this should be continued for two cycles or until each portal has received 400r. By this time noticeable regression should have occurred and the debilitating effects of radiation can be lessened without greatly inhibiting the rate of tumor shrinkage by decreasing the daily dose to 100r and continuing with the other factors as before. When the tumor has nearly or quite disappeared, nephrectomy should be performed. Although tumors diminish in size at different rates the majority of patients can be operated upon within a month and some considerably sooner. Tumor disappearance has been noted after 800r had been given each of three portals.

The general condition of young patients under irradiation must be carefully watched. An examination should precede each treatment. Blood counts should be made on alternate days and transfusions given if anemia occurs or if the white cells fall much below 2,000 per cubic millimeter. The tumor is measured daily and excretory pyelograms are taken every seven to ten days. Chest films should be taken every ten days until the patient leaves the hospital and at reasonably short intervals for the following year.

Removal of irradiated Wilms' tumors is not difficult in most cases but the greatest care must be taken to prevent puncturing of the tumor capsule and spilling the contents in the wound. If this accident occurs, local recurrences almost invariably follow. Such a disaster is a clinical demonstration of what the microscope has repeatedly shown in these cases when some viable tumor tissue can be recognized, although by far the greater portion has become necrotic.

About two months after nephrectomy another cycle of irradiation should be given. One hundred *r* is given a portal daily until 2,000*r* has been received by each of three portals. During this treatment the patient requires the same close observation as when the pre-operative radiation was given. Sufficient experience has not accumulated for the value of post-operative irradiation to be known. Obviously, if all the disease were removed by operation, subsequent irradiation would be unnecessary, but personal experiences and those of others suggest that cures are practically unknown even when irradiation sufficient to cause marked tumor shrinkage has been given and an apparently complete operation has been performed.

If treatment is given with radiation alone, the dosage should be divided so that a cycle of long duration can be tolerated. Daily treatments of 75*r* or 100*r* should be given to one of three portals until 3,000*r* has been applied to each. In children about three years old and of average size about 7 threshold erythema doses will be delivered to the region of the renal pedicle by this amount of treatment. Such a cycle may control the disease.

The treatment of metastases depends upon their location. The lungs and the brain seem to be most frequently affected. It is not unusual for patients to have metastases at the time of their first examination. In all such cases complete reliance must be placed upon radiation. Treatments should be given to all affected regions in turn and great care must be used to obtain tumor regression without over irradiating the patient. In these cases especially, blood transfusions are helpful.

ADENOCARCINOMA OF THE RENAL PARENCHYMA IN ADULTS

While the unqualified statement can be made that radiation should play an important part in the treatment of all Wilms' tumors, the writer believes that as yet radiation has proved of but slight clinical value in the management of adenocarcinomas of the renal parenchyma in adults. This statement unfortunately conflicts with a number of more optimistic reports in the literature.

The writer believes that the following conclusions represent a fair estimate of the present value of radiation in the treatment of adenocarcinomas of the renal parenchyma in adults:

1. Radiation alone can not be depended upon to control this disease.

2. Pre-operative irradiation will cause regression in the size of the majority of these tumors. This may greatly facilitate nephrectomy. The value of radiation alone in such cases is approximately equivalent to partial removal of the tumor.

3. Irradiation will not make an inoperable tumor operable. A tumor is considered inoperable when it has perforated the renal capsule and invaded the perirenal tissues. Large size alone does not make a tumor inoperable because the surgeon's skill is such an important factor.

4. If tumor cells are disseminated by the unavoidable trauma of a skillfully performed nephrectomy—and this has not

been proved—a pre-operative cycle of radiation will not prevent the disaster.

5. During the course of a pre-operative cycle of irradiation and the period of waiting for its effects to be established and regeneration of the superficial tissues to take place, metastasis may occur.

6. If a tumor recurs locally even though it appears to be superficial, external irradiation may diminish its rate of growth but will not stop it.

7. Metastases from these tumors show great differences in their radiosensitivity depending on their location. Secondary deposits in the lungs have completely disappeared while those in bones are inhibited slightly, if at all.

All known diagnostic aids should be used in studying these patients and determining the exact status of the local tumors and detecting metastases, if present in other parts of the body. In addition to the usual diagnostic procedures, aspiration biopsy and perirenal insufflation are frequently of great value. In some cases the history is most helpful. It is well known that these tumors tend to grow into the renal pelvis and cause hematuria and that when they are discovered shortly after the onset of hematuria many of them are operable. It is quite different when patients seek medical advice for loss of weight and progressive weakness and a renal tumor is discovered because in these cases the primary tumor is usually inoperable, since the growth, rather than eroding the pelvis, has perforated the capsule and has continued its development in the perirenal tissues.

If the urologist decides to give pre-operative irradiation, the following factors have proved effective: the 200 kilovolt unit, filtration of 2 millimeters of copper, a target skin distance of 70 centimeters and three renal portals, anterior, lateral, and posterior, each about 10 by 14 centimeters in size. A single portal is given 250*r* daily until each has received 2500*r*. This treatment requires about a month and delivers to the region of the kidney pedicle about 5 threshold erythema doses in a man of 150 pounds (68.2 kg.) weight. After studying the radiation required to control other somewhat similar tumors—for there is no definite information regarding renal adenocarcinomas—it seems reasonable to estimate that this is somewhat less than half of a curative dose. In most cases there is superficial blistering of the skin but healing is complete in about six weeks. At the end of this time (or two and one-half months after irradiation was started) nephrectomy can be performed with little if any noticeable delay in the healing of the wound.

If the kidney tumor is judged inoperable and treatment is given by irradiation alone, the maximal dose should be delivered. In these cases it is not as important to keep within a time limit or so carefully to preserve the skin. Four portals are suggested, each about 10 by 14 centimeters in size, the other factors remaining the same as in the pre-operative cycle. With an additional portal one more day intervenes between successive exposures of each portal and greater skin regeneration takes place between treatments. As a result it is often possible to increase the total dose to 3000*r* or even more to each portal. This furnishes about 7 threshold erythema doses to the region of the renal pedicle in a man of about 150 pounds. In certain favorable cases, after a rest period of two to three months, additional irradiation may be possible but there is great danger of seriously injuring the superficial tissues.

While these doses of radiation are tolerated by most adults, the general condition of the patients should be carefully observed. Care must be taken to keep the quality of the blood high because anemic individuals do not respond favorably to irradiation. A diet rich in liver or liver extracts is helpful but transfusions of whole blood are best.

Irradiation of metastases from renal adenocarcinomas is interesting because of the great variation in radiosensitivity shown by these growths in different parts of the body. Bone metastases are among the most aggressive tumors known. They cause rapid destruction in the bone of their

origin with slight tendency to bone regeneration and will cross joint spaces to invade adjoining bones and adjacent soft parts. Lung metastases, in contrast, are frequently controlled with moderate doses of external irradiation.

PAPILLOMATOSIS AND EPIDERMOID CARCINOMAS OF THE RENAL PELVIS

Radiation is not recommended in the management of these diseases because complete devitalization of the tumors is unlikely. In addition the kidney is invariably infected before the diagnosis is made and its function is usually hardly worth preserving. For these reasons and because in most cases the disease is confined within the kidney and ureter, with perhaps occasional bladder extensions, nephroureterectomy (including a cuff of bladder mucosa surrounding the ureteral orifice) should be performed as soon as possible after the diagnosis has been made. Sometimes these patients are in such poor general condition that the operation is best performed in two stages. The kidney with the greater portion of the ureter can first be removed and six to eight weeks later the operation can be completed. For the first stage, the usual loin incision extended as much as necessary is quite adequate. The writer recommends a pararectus incision for the second stage as being much more convenient than the usual suprapubic mid-line approach.

Because of the well known tendency of the mucous membrane of the entire urinary tract to develop papillomatosis, after papillomas have been removed with one kidney and ureter the bladder and remaining kidney and ureter should be closely observed for years. Growths appearing in the bladder can be controlled by cystoscopic fulguration, but when tumors spring up in the single kidney or ureter the best that can be hoped for at present is temporary palliation by irradiation.

A mistake was recently made by the writer and it is described to illustrate the diagnostic difficulties which these tumors occasionally present. A frail man who had had a papilloma removed from his bladder was referred because of persistent hematuria. The bladder was found to be normal but the radiographic picture of one kidney and ureter showed either papillomatosis or pyelitis and ureteritis cystica. A catheter was passed up and down the ureter to loosen tissue and suction was applied to draw the fragments into the catheter. Material was obtained and the smears were stained and studied under the microscope by a competent pathologist. His diagnosis was papillomatosis. When the kidney and ureter had been removed, only cysts were found but the cyst walls were composed of so many layers of epithelial cells that the diagnosis of papilloma seemed justifiable when only isolated fragments were provided for examination.

CONCLUSIONS

1. In the management of Wilms' tumors, radiation should play the principal role. Probably if all operations upon these patients were abandoned and full doses of radiation substituted, the survival rate would greatly improve.

2. Radiation will diminish the size of most adenocarcinomas of the renal parenchyma in adults and will often control lung metastases from these tumors, but other benefits of this treatment are questionable.

3. Irradiation is not recommended in the management of papillomas or epidermoid carcinomas of the renal pelvis and ureter. Prompt radical surgery followed by long periods of close observation is the treatment of choice.

4. If future progress in irradiation is as rapid as that of the past ten years, it is likely that before long the agent will play a much more important part in the treatment of renal tumors than has been indicated in this paper. However, all estimates of the value of radiation must be based upon clinical experiments which have been carefully performed and critically studied.

THE INCIDENCE AND PREVENTION OF RENAL AND VESICAL CALCULI IN THE FRACTURE AND TRAUMATIC GROUP*

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WHEN requested to make a contribution to the Urological Symposium for the present number of the American Journal of Surgery, the Editor suggested that we examine the problem of calculus formation in the fracture and traumatic group and further that we confine our presentation to the question of *incidence* and *prevention*.

We have previously discussed the problem and stated our experience with it at a meeting of the Pennsylvania Medical Society in October, 1935, and later before the American Association of Genito-Urinary Surgeons, May 26, 1936, at Stockbridge, Massachusetts.

To summarize or quote from this paper. In our presentation we took the position that stone formation in the fracture and traumatic group is a practical *clinical problem of major importance*. It is important for the reason that an increasing number of patients, stonefree on admission, with simple or compound fracture or osteomyelitis, develop calculi during their hospitalization—many with grave damage to one or both kidneys—the latter overshadowing in gravity the lesions for which they were admitted and from which they might have recovered with little or no functional impairment. Unfortunately, in the past we were only asked to see these patients *after* they had developed evidence of urinary tract complications. We think this is probably true in the majority of fracture services.

Ten cases were reported in the first paper, and as an illustration of the gravity of the complications in that group, we recited that one of the group, admitted with fracture of the 4th and 5th lumbar vertebra, very mild and transient cord symptoms, normal urine acid in reaction, *x*-rays negative for stones, catheterization necessary only for the first forty-eight hours, was confined to bed six months; during that time he developed such extensive bilateral calculi that death occurred from uro-sepsis. Of the remaining nine, three had bilateral stones removed by pelvio-lithotomy; four, unilateral (in three the destruction so great that conservative surgery was not possible, and we were obliged to employ nephrectomy). In one, a boy with a long-standing, unrecognized osteomyelitis of both femurs, sent in from a small suburban hospital, there was extensive calculosis of left kidney, requiring nephrectomy. The two remaining cases had multiple vesical calculi removed by cystotomy.

There was no mortality in the nine operated case. In the ten cases, the complications occurred in six, with fracture of the bony pelvis: two with fractures of the lumbar spine without cord injury; one with osteomyelitis of both femurs; one with a rupture bladder and perforation of the rectum. With the exception of the boy with the osteomyelitis who developed ankylosis of both hips, there was no function impairment as a result of the primary injury. The only death was due to complications that we felt might have been prevented. Since reporting these cases we have seen five more, two with fractures of the lumbar spine, three with fractures of the pelvis.

No attempt will be made to examine into or speculate on the genesis of nephrolithiasis, nor to review in summary the

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splendid contribution to this subject on the investigative side, by such workers as Randall, Higgins, Keyser etc., the group at the Mayo Clinic, or the extremely interesting and stimulating studies of Albright, Barney and their associate workers at the Massachusetts General, on the subject of stone in relation to hyperparathyroid activity. The contribution of this group, as well as those of McCarrison and the Continental workers, is familiar to all who are interested in this problem, and while the *causus actualis* has thus far eluded them, their carefully documented findings and observations have put into the hands of the clinician who is interested in the practcial side of the problem, extremely valuable information for use in the *prevention* of *formation* in the group under discussion, and in the treatment and prevention of re-occurrence in those already afflicted. From the investigations of these workers we feel that eventually will be written one of the finest chapters in preventive medicine.

INCIDENCE

Actual statistical incidence is difficult, if not impossible, to establish from careful examination of the literature on the subject. As a rule, they are reported as isolated cases described as complications occurring in fractures of the lumbar spine, bony pelvis, femur and in cases of osteomyelitis. No attempt is made to establish the relation between the group that develop calculi and the number of fracture cases admitted. In many of the cases the data is inadequate, and the unavoidable errors that get into any clinical observation such that deductions as to the sequence following the injury can only be of speculative value.

It is of extreme importance in the study of this group to have definite information as to the presence of pre-existing renal lesions at the time of injury; this information is absent in the report of many of the cases.

One might cite as an evidence of the frequency of occurrence, the experience of Conwell who reports ten cases—10 per cent in a series of 100 cases—of fracture of the lumbar spine without cord involvement. In a personal communication he states that the stones were found from ten to twelve weeks following injury, and feels that trauma is a very important factor in their formation. He does not attach much importance to the question of stasis in the group. Few of his patients are in bed any longer than four or five weeks and are moved frequently.

In 1895, Mueller from the Halle Chirurgical Clinic, reported eight cases of extensive bilateral nephrolithiasis occurring in ten cases of fracture of the lumbar vertebra with paralysis of the cord. He describes with fine clarity the clinical picture so commonly observed in this group and commented on by most observers.

The symptoms usually occur between the third and eighth week; the sudden and dramatic appearance, without apparent cause, of rigors, fever, lumbar pain and tenderness, frequently a dysuria, the first renal or vesical outcry announcing the presence of a serious urinary tract infection, and invariably an infected alkaline urine. This picture is not infrequently interpreted as an acute pyelitis and treated as such.

This may lead to serious consequences, for if stones are not already present the stage is properly set for their formation, as all of the underlying factors so frequently observed in stone formation are present—i.e., stasis, alkaline infected urine (frequently with a urea-splitting organism) and the marked increase in the urinary calcium that occurs in immobilized fracture cases.

Numerous other writers from Mueller down to the present have recorded their observations in this group. One of the noteworthy contributions was that of E. H. Paul, who reported twenty cases of stone formation in gunshot wounds of the femur with suppuration: in all, the presence of an alkaline infected urine, the stones composed of calcium phosphates

and carbonates. Sisk, Holmes and Coplan, O'Conor Herman, Harper, Joly, Cabot and others.

Goldstein and Abeshouse, in an article in the *Archives of Surgery* in December, 1935, made a careful survey of literature and reported fourteen cases. In a recent communication, one of the authors (Abeshouse) stated that since the publication of the paper, he has seen eight additional cases. Six of the group fall into the fracture and traumatic group, the other two in cases of osteitis deformans. He writes: "I am inclined to believe the most important factor in the production of stones in the various bone diseases is;(1) disturbance of calcium metabolism; (2) preexisting lesion of the kidney which results in the faulty excretion of urinary salts."

Higgins, in an article in the *British Journal of Surgery*, March, 1937, states that in the past year he has seen six patients in whom stones had developed during prolonged hospitalization due to an orthopedic condition. The stones were composed of calcium phosphates and carbonates.

There is only an occasional reference in the literature to the occurrence of urinary calculi in association with bone disease in children. This is somewhat surprising in relation to the number that are immobilized for long periods, and in whom there is a high incidence of "deficiency disease."

Borman reviews the literature and reports one case. Leon Herman in a discussion of Paul's paper, reports a case of stone formation following osteomyelitis of the right tibia in a boy aged 8. The only other reports in this review are those of the French surgeons, Mayet and Bonneau.

In a personal communication, Charles Mixter writes of his observations at the Childrens Hospital in Boston; "We had a number of cases in childhood who were on Bradford frames for long periods of time, or immobilized in other methods, who developed urinary calculi and I feel as you do that it is an important problem to recognize and combat."

Except in Conwell's group, one cannot allege that the incidence of stone formation in this group is high. We have corresponded with surgeons who have charge of large industrial services in this country. George Davis of Chicago, J. H. Wagner of Pittsburgh, both with large traumatic services, report that they rarely see it as a complication. Phemister, of the University of Chicago, writes that it is a development that he has not seen, but that it is possible that a review of histories would reveal its occurrence oftener than could be accounted for by coincidence. We have taken the position at Mercy that while the incidence may not be high, the gravity of the complications may be so serious that we have set up a programme designed to prevent what would seem to be the contributing factors in stone formation in this group.

PREVENTION

In our plan, through the courtesy and cooperation of the Surgical Division, we are asked to see these patients on admission. We have classified the potential stone-formers as follows:

(a) Fractures of spine with or without cord damage.
(b) Fractures of bony pelvis with or without rupture of urethra or bladder. (Complications are not uncommon in this group)
(c) Fractures of femur, simple or compound.
(d) Osteomyelitis.

On Admission: (1) Roentgenogram of urinary tract to determine presence or absence of calculi. (2) Careful examination of urine to establish presence or absence of infection. *p*H. (daily), Jean's test.

Chemical Studies: Consisting of the determination of serum calcium phosphorous protein and phosphatase. This is repeated at short intervals. In the event of the elevation of the serum calcium and lowering of the phosphorous, the patient is then studied from the standpoint of hyperparathyroid activity. This has *not* been observed in any of our patients

in this group so far. The blood calcium figures are rarely elevated. Blood chemistry in terms of non protein nitrogen, urea, creatinine, are generally within the normal range. Bone repair in this group is apparently not affected by marked degrees of decalcification.

Diet: We have taken the position that if we can maintain the chemical equilibrium of the urine at a *p*H level of between 5 and 5.5, the precipitation of the calcium phosphates and carbonates will not occur. This we have been able to accomplish with a high vitamin acid ash diet. The patient is individualized, the *p*H examined daily, the constituents of the diet varied with changes or fluctuations in the *p*H. In the majority of cases the diet, without acidifying medication, was sufficient to maintain the hydrogen ion concentration to a level between 5 and 5.5. In a few of the cases it was necessary to supplement it by the administration of ammonium chloride, enteric coated tablets, grains 7½, two tablets four times daily.

In the problem of prevention in this group it is extremely important that all alkaline medication is interdicted.

Stasis: An attempt is made to minimize the effects of stasis in the immobilized patient by frequent movement and elevation of the renal level, consistent with the treatment of the particular case. The practice of some surgeons in minimizing recumbency in lumbar and pelvic fracture is of extreme importance in this respect.

Infection: All instrumentation is done with extreme care, with the most rigid asepsis. These cases are under constant supervision of the Urologic Department, and particular attention is paid to the prevention of overdistention of the bladder (in the non-paralytic cases).

Fluids are forced to a minimum of three litres per day in the uninfected cases.

As soon as evidence of infection in the urinary tract occurs, expressed in terms of a pyuria, the bacteriology of the infection is established, and specific measures instituted at once to combat the infection.

The studies of Helmholz—of the effects of mandelic acid therapy in the bacillary infections—have been of inestimable value and in the cases where there is no evidence of renal insufficiency, a carefully controlled plan for its exhibition is put in operation. The recent studies in the use of Prontylin in the coccal infections are also of value. It is of extreme importance that all the measures for prevention and care of these cases be carefully controlled by the physician and dietitian in charge of the case, as the rationale of the care is predicated on the hydrogen ion concentration of urine and the bacteriology of infection when it occurs.

In the past ten months, with the plan as outlined, we have been able to maintain the chemical equilibrium of the urine in the following group of patients admitted in the Fracture Division of Mercy Hospital.

10 cases: Fractures of the spine, uncomplicated

3 cases: Fractures of the spine, with cord involvement.

12 cases: Compound fracture of femur

3 cases: Fracture of pelvis

3 cases: Osteomyelitis of the femur

2 cases: Osteomyelitis of the tibia

We do not allege that if this plan had not been carried out, these patients would have developed calculus. We do feel, however, that it is an important prophylactic measure, and that a well organized urologic service can be of valuable assistance to the fracture service in the prevention of grave urinary tract complications.

CONCLUSION

(b) The incidence of stone formation in the fracture and traumatic group is examined, from a review of the literature.

(b) A plan for prevention is outlined. With this plan in operation we have been able to maintain the hydrogen ion concentration of the urine at a level where the precipitation of calcium phosphates and carbonates does not occur.

The plan is submitted as a useful prophylactic measure in the potential stone-formers of the fracture group.

COMPLICATIONS FOLLOWING PROSTATIC RESECTION

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THE majority of complications encountered after transurethral resection, like those following prostatectomy, group themselves naturally into four divisions: 1, complications that are the result of incomplete relief of urinary obstruction; 2, complications directly attributable to loss of blood; 3, complications that develop as a result of infection; 4, complications arising from impairment of the cardio renal vascular system. While these complications are similar to those encountered after prostatectomy, I believe I may state without fear of contradiction that both their incidence and severity are less following resection and explain its lower mortality rate.

Due to its peculiar technique, a fifth division might be added which was seldom encountered after prostatectomy but is seen too frequently following resection. I refer to the various forms of periurethral infection resulting from a combination of urethral trauma and sepsis. While this last group of complications rarely prove lethal, they unduly prolong convalescence and not infrequently result in permanent damage to the urethra.

COMPLICATIONS RESULTING FROM OBSTRUCTION

The operation of resection, like the majority of surgical procedures upon the urinary tract, is intended primarily for the relief of urinary obstruction. If the obstruction is only partially removed, the desired relief is not obtained and the persisting obstruction, plus the trauma incident to the operation, are prone to result in an ascending infection followed by a more or less severe febrile reaction. It is imperative, therefore, that the operative procedure leave the patient with an unobstructed urethra. If this is not possible because of the great amount of tissue to be removed, then it should be accomplished either by the use of an indwelling urethral catheter or by suprapubic drainage. Experience has shown that where it is not possible to remove all of the obstructing gland at the first operation the remaining portions may be resected within a week. This usually produces less reaction than occurs following the initial procedure, due undoubtedly to protective barriers thrown up in the adjacent prostatic tissue since the first resection. It is common experience that tissue access to which was difficult at the first operation can now be readily removed as a result of its enlargement by subsequent edema. There should be no hesitation, therefore, in completing the removal of the gland within a week of the first operation, and longer delay has no advantage and may prove detrimental.

While the necessity of carrying out the procedure in multiple stages need lead to no complications, failure to completely remove the obstruction will certainly do so. When such complications develop, they are frequently due to failure on the part of the operator to resect those portions of the lateral lobes nearest the veru montanum. The proximity of the external sphincter to this area may cause the operator to be overcautious. Such caution, while commendable, must not be carried to the extent of leaving this portion of the hypertrophied gland intact, for here the urethra narrows, and the presence of even small remnants of prostatic tissue may prevent the free passage of urine. Such a complication can best be avoided by having an assistant place his finger in the rectum; and by

elevating this portion of the urethra the resection of these terminal ends of the lateral lobes is facilitated. Occasionally a hyperplastic anterior lobe is overlooked and, if not removed, may produce similar complications. The routine use of a retrograde lens system is the best insurance against such a complication. In those cases where the hyperplasia of the prostate has elevated the trigone, good functional results are only obtained when this portion is adequately resected, even up to and including the interureteric ridge.

While much emphasis is placed on the complete removal of the obstruction in the avoidance of complications, it must be remembered that the same cause and effect will operate if the tubular drainage following operation is not properly cared for during convalescence. Many post-operative difficulties can be avoided if time is taken to adjust carefully the indwelling catheter at the completion of the resection, being sure that it drains freely and completely empties the bladder. In order to permit the free discharge of urethral exudate along its walls, such a catheter should be of as small calibre as is consistent with satisfactory drainage. A number 22 French has been found the size most generally applicable. The adhesive strips which hold it in place must be brought up well over the pelvis in order to insure firm anchorage, and should be attached to the catheter in such relation to the external meatus as to permit free escape of the urethral discharges. Such obstruction is frequently the source of unexplained fever. It is well also to use a catheter with multiple holes extending over several centimeters of its distal end. One need hardly emphasize that it should be of soft consistency in order to cause as little trauma as possible. When most patients leave the operating room, their after-care becomes a routine procedure with which the nursing staff of all recognized hospitals is assumed to be familiar. Therefore, the surgeon may expect that what complications may occur will be met by the hospital personnel in an established manner. In the case of such a comparatively new procedure as transurethral resection, methods of post-operative care have not been so well standardized. There is no external wound with its associated dressing to impress upon the nursing staff the seriousness of the operative procedure just completed, and catheters are likely to be regarded with distaste and examined as seldom as possible, especially when they occupy the male urethra. The fundamental principle of free and uninterrupted drainage of the urinary tract, if appreciated at all, is usually totally disregarded until the bladder has become distended to the point of extreme discomfort, at which time the nurse usually does not seek to relieve the obstruction but starts on a prolonged and often futile search for an orderly. In the interim there has occurred a reflux of urine to the renal pelvis resulting in an ascending infection with its associated chills and fever of greater or less severity, depending on the virulence of the infecting organism.

COMPLICATIONS RESULTING FROM INFECTION

It is imperative that all catheters, tubes, and receptacles employed in drainage following transurethral resection be surgically clean. Sterilization of rubber tubing is frequently inadequate, and many complications attributable to infection could be avoided if rubber tubing were properly sterilized. Placing catheters and tubing in boiling water insures sterilization *only* of their exterior. The air locked in their lumen insulated by the walls of the tube prevents the destruction of the bacteria. Only by immersion in a germicidal solution so that the liquid flows to all surfaces is adequate sterilization obtained. Having observed the recognized aseptic technique while in the operating room, to place the patient's urethral catheter upon his return to bed in a urinal is to defeat absolutely the purpose of the operative room asepsis and insure the rapid passage of noxious organisms through the catheter lumen into the

bladder. All indwelling urethral catheters should be connected to at least three feet of sterile tubing and drained into *corked* by sterilized equivalents at least once in every twenty-four hours, one's eyes detect the encrustation of urinary salts not alone

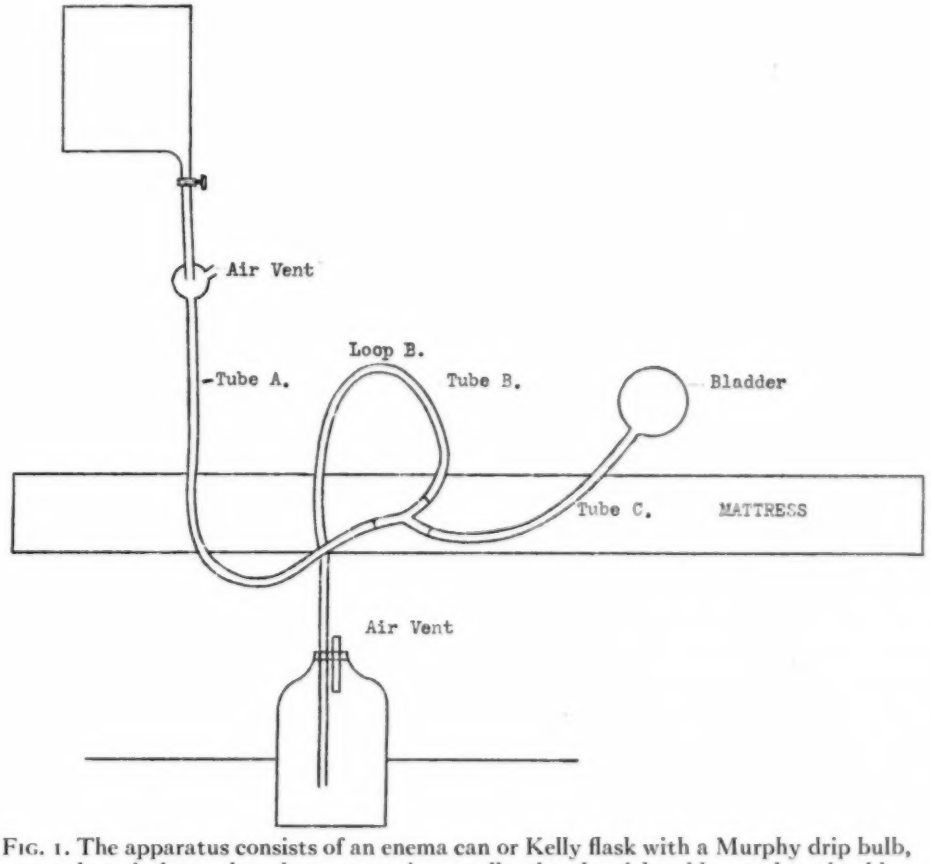

Fig. 1. The apparatus consists of an enema can or Kelly flask with a Murphy drip bulb, a Y-shaped glass tube, glass connections, gallon bottle with rubber cork and rubber tubing. The Y-shaped tube should be turned so that air entering through the air vent will flow through Tube A into Tube B, and then into the bottle. This prevents the bladder from filling with air. If this occurs, irrigating fluid will not enter the bladder. The amount of positive pressure applied to the bladder during the filling phase is determined by the height of loop B above the bladder. The amount of suction is determined by the length of Tube B below bladder level, and is governed by raising and lowering the bottom bottle.

sterile bottles. Such bottles should be of at least a gallon capacity, in order that their infrequent emptying may permit their replacement daily by recently sterilized equivalents. If they are smaller, the necessity of frequent replacement will encourage the nursing staff in such slovenly habits as placing the end of the tubing on the bedding or allowing it to drag on the floor while the receptacle is being emptied, instead of being replaced.

In those hospitals where it is not compulsory to replace all urinary receptacles on the sides of the receptacles but frequently in the wounds, while one's nostrils are offended by ammonia. This is the product of urea splitting bacteria in the urinary tract and may be likened to rats in a house, a presumptive indication of filth and negligence. In such institutions it is not an infrequent occurence to find that the aged prostatic, while wearing an indwelling urethral catheter, is permitted to go to the toilet to defecate unaccompanied by an attendant. He will naturally and invariably thrust the end of his catheter carefully into

the toilet bowl where it dangles amidst the excreta, the contamination from which is propelled into his urinary tract at the time of his next bladder lavage. The source of a later intractable cystitis remains an unsolved mystery to his attending surgeon who, while observing the most meticulous operating room technique, seldom inquires into routine after-care in his wards.

To overcome these difficulties, I have used for the past three years in my private practice what I term the mechanical nurse. (Figure 1.) This insures the constant and regular irrigation of the bladder for the first forty-eight hours after resection with a mildly germicidal solution in a closed system, so there is no opportunity for the introduction of foreign organisms. Those suffering from prostatism, because of past febrile reactions, tend to become immuned to those organisms to which they are host, even when these are stirred up by the trauma incident to the removal of their habitation by resection.

Few, I think, appreciate how easily organisms not common to the host gain entrance to the urinary tract, and how much more serious are the complications they are capable of causing. It is essential, therefore, that every effort be made to prevent their introduction, and nothing is so likely to cause such introduction as the frequent irrigations of the urethral catheter with a syringe. This danger is eliminated to a large extent if the urethral catheter is always kept attached to a closed receptacle such as the "mechanical nurse" or is simply attached to a corked sterile bottle by a yard of sterile tubing when lavage of the bladder is not indicated.

When proper attention is given to the sterilization and care of urinary drainage apparatuses, these patients may occupy double rooms without giving the least olfactory offense to their room companion. Disturbing urinary odors are a positive indication of poor nursing care or improper sterilization of apparatus and bears a direct ratio to the frequency of fever and the length of convalescence.

The recent advances made in rendering the urine germicidal by an increase in its acidity should not be neglected in the prevention of infection; but more important are measures intended to prevent introduction of bacteria rather than their destruction after they have entered the urinary tract.

Statistics show that epididymitis occurs with prostatism in 15 to 20 per cent of all cases. This complication, which is invariably associated with seminal vesiculitis, has not infrequently proved lethal. As its prevention is absolutely assured if a partial vesectomy is performed, there seems to be no valid excuse for its omission.

COMPLICATIONS RESULTING FROM TRAUMA

Periurethritis of varying degrees together with periurethral abscesses, fistulae, and late strictures, are complications particularly prone to follow transurethral resection. They are entirely attributable to the technique of this new procedure and occur undoubtedly in much greater frequency than is generally appreciated. The urethral mucosa is capable of withstanding much manipulation if kept well lubricated—otherwise very little. The desire to remove as large pieces of tissue as possible during the procedure has resulted in the manufacture of resectoscopes which are in diameter very close to, and in some cases beyond, what can be safely inserted in many urethras and leave any space for proper lubrication between the outside of the sheath and the mucosa. When an instrument can not slide back and forth in the urethra with ease the mucosa is being traumatized, and if such trauma persists over an extended period of time, periurethritis will develop, to be followed by abscesses, fistulae, and stricture, depending on the duration of the trauma and the type of the associated infection.

To facilitate the passage of the resectoscope, the custom of dilating the urethra with sounds prior to its introduction has become the routine procedure of some

operators. Unless great care is taken, the urethral mucosa may thus be severely traumatized at the very start of the procedure, which the subsequent manipulation tends to aggravate. When this happens, by the time the operation is completed, the mucosa may be so extensively injured that during subsequent healing large areas of scar tissue form. The patient then finds himself with a new type of urinary obstruction in the form of a urethral stricture in place of the prostatic obstruction for the relief of which he underwent operation. While his former type of obstruction was curable, this newer type will require periodic treatment the rest of his life.

In most cases following urethral meatotomy, standard resectoscopes will pass without undue trauma if the urethra has been properly lubricated. The fact that such lubrication is sufficient for the introduction of the instrument does not mean that it will suffice during the entire procedure. Good technique demands that as soon as the instrument fails to slide back and forth easily it should be removed at once and re-lubricated.

The trauma caused to the urethral mucosa, in many cases, would without doubt heal satisfactorily were it not for the necessity of insuring continuous urinary drainage immediately after the operation by the use of an indwelling urethral catheter. This naturally tends to interfere with the proper and adequate drainage of the inflamed surface, and for this reason the catheter chosen should as previously stated, be of as small diameter as is consistent with free drainage, and removed as soon as bleeding has ceased, usually at the end of forty-eight hours. If these precautions before, during, and after operation, are observed, the incidence of periurethral abscesses, post-operative strictures, and urethral strictures, will be few. A large enough series of cases has been operated upon by us without such complications to demonstrate that they are the result of carelessness in technique and not a necessary sequel of the procedure.

COMPLICATIONS DUE TO BLEEDING

Probably no one factor so long delayed the development of transurethral resection as the inability satisfactorily to control bleeding. A method for removing tissue through the urethra was available in the form of Dr. Young's Punch for nearly twenty years before the technique for controlling the associated bleeding by the use of diathermy currents was perfected. How excessive the loss of blood may be even with this means of hemostosis Pilcher and Sheard[4] recently demonstrated. They found in one series of fifty-five cases that it amounted to 39.03 c.c. per gram of tissue removed, and in a second series 22 c.c. If we accept 30 c.c. as an average, it becomes apparent how important a factor such a loss is when we consider that for the average case between 15 and 20 grams of tissue must be resected adequately to remove the obstruction.

These figures are based on the removal of tissue by the tubular knife method, and it is fair to assume that with the loop electrode method the loss of blood is considerably less. This diminution in blood loss, however, is effected by a greater destruction of tissue through coagulation, and hence tends to increase the chances of subsequent bleeding during convalescence when the eschar finally comes away. Excessive destruction of residual prostatic tissue by electrocoagulation not alone delays healing through the devitilization of the immediate tissue involved, but has recently been demonstrated by Flocks[3] to be an important factor in the production of chronic infection through the destruction of the blood supply to other parts of the gland. He has shown that the chief blood supply of the hyperplastic portion of the gland enters at the vesicourethral junction through multiple arteries grouped near the apex of the trigone. These penetrate the gland parallel with the urethra. If sufficient coagulation has been applied to the vesical edge to destroy these main vessels, that portion of the hypertrophied gland nearer

to the veru montanum will be rendered avascular. When this part of the gland has not been adequately resected, as referred to earlier, its healing will be slow and protracted; and not infrequently an area of sloughing prostatic tissue incapable of healing will remain to act as a constant source of infection and irritation.

If a patient bleeds after suprapubic prostatectomy, there is always a suprapubic opening through which clots may be exuded and pressure be relieved. Not so in the resection case. If the catheter or urethra becomes obstructed by even a small clot, when the bladder fills it will contract in an attempt to expel it, ineffectual spasm of the bladder musculature will develop, and the bleeding, which was at first insignificant, becomes aggravated. More clots form, which the bladder tries vainly to expel, and so a vicious circle is established which might have been prevented by the prompt opening of the obstructed catheter when first occluded. In such a case, there is nothing to be gained by watchful waiting in the hope that the bleeding will stop. It will continue until the bladder has been cleared of clots, and frequently on their evacuation, the bleeding ceases spontaneously. To the inexperienced, bleeding is a formidable and serious matter necessitating transfusions and even cystotomy. The stopping of such bleeding by transurethral methods requires the maximum of technical skill, and those who have not attained such skill will resort to opening the bladder suprapubically. To have informed a patient of the benign nature of transurethral resection, and having undertaken it, to be compelled to perform a suprapubic cystotomy after an ineffectual attempt to control post-operative bleeding, is likely to cool the ardor of the most enthusiastic resectionist. But if the axiom that an empty bladder is the best insurance against hemorrhage has been conscientiously followed through convalescence, such trying experiences will prove rare.

COMPLICATIONS, THE RESULT OF CARDIORENAL VASCULAR IMPAIRMENT

The fact that transurethral resection is associated with little shock makes it possible to relieve many patients with greatly reduced renal function and impaired cardiovascular systems of their urinary obstruction who would be considered too poor a risk for prostatectomy.

The pioneers in prostatic surgery found renal insufficiency to be the most frequent cause of serious complications. Efforts to overcome it are largely responsible for the development of our various tests of renal function, as well as for our appreciation of the advantages of pre-operative drainage and the intravenous use of fluids. Today the risk involved from the standpoint of reduced renal function can be gaged so accurately that one can feel relatively certain that if other complications do not occur this impairment need not prove of great consequence. Even before resection became popular, many felt that cardiovascular renal disease no longer constituted the chief cause of serious complications following urological surgery. Cabot,[2] writing on the subject in 1931, stated; "Renal insufficiency presenting the picture of nausea, vomiting, distention and somnolence is not common and has probably fallen from first to at least fourth place." The appreciation of this fact has resulted in the average age of patients undergoing resection, being considerably higher than those treated by prostatectomy. Alcock[1] reports that 65 per cent of his patients undergoing resection are over 70 years of age. In my own cases, 49 per cent have been over 70. Only those who have observed many cases can appreciate how little the demands on an impaired renal function are increased by resection, provided sepsis is avoided.

Patients who have a history of impaired cardiovascular function, as exemplified by previous attacks of angina, are prone to acute exacerbations of this condition if a marked fall in blood pressure occurs. This

fluctuation in blood pressure, I believe, is generally the result of blood loss during or following operation, with its associated anaxemia of the heart muscle rather than the direct result of the anesthetic, or any shock associated with manipulation of the posterior urethra.

In conclusion, it would seem pertinent to observe that the complications of resection can best be prevented by avoiding trauma, and insuring unobstructed drainage with the rigid application of aseptic and antiseptic technique.

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The extremely poor outlook for patients suffering with tumors of the testicle is well recognized. Orchidectomy, even with early diagnosis, is a dismal failure. . . . A mortality after surgery of over 80 per cent is appalling, . . . that castration must be supplemented by radium, Roentgen ray or more radical surgery is apparent if any considerable improvement in treatment is to be gained.

From—"Modern Urology" Edited by Hugh Cabot, M.D., C.M.G., F.A.C.S.

CHRONIC ABSCESS OF THE PROSTATE GLAND

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ALMOST every physician thinks the term abscess of the prostate gland refers only to an acute suppurative process evidenced by fever, chills, dysuria and other severe local or systemic symptoms. While this is an important clinical entity it occurs infrequently and it seems important to call attention to the fact that the type of abscess most often encountered, though not always recognized, is chronic prostatic abscess, single or multiple, which exists for years, seldom causes an acute febrile episode, but which nevertheless is primarily or secondarily responsible for very definite disability. This paper will deal only with the latter variety of prostatic abscess.

In 1933, I described a condition termed chronic abscess of the prostatic ducts and outlined a method of treatment. A later article discussed a group of sixty-seven cases of this type for which transurethral operations were performed at The Mayo Clinic during a period of three years. Since then several additional cases have been subjected to operation, bringing the total number of cases by January 1, 1937, to 149.

ETIOLOGY

A number of years ago Alexander in a reasonably large series of cases of gonorrheal urethritis found many in which the infection had extended back into the prostatic urethra and caused single or multiple small abscess pockets at various depths within the prostate gland. He believed the occurrence of such lesions was the rule in gonorrheal urethritis rather than the exception. If this be true it seems in many cases that the areas heal spontaneously or else, considering the incidence of gonorrheal urethritis, more cases of chronic abscess of the prostate would be encountered. Making some allowance for the poor memory of some patients it is possible that an antecedent Neisserian infection has existed in the majority of cases of chronic prostatic abscess which I have observed. However, I am fairly certain that not all cases have a gonorrheal etiology, for in a number of cases the chronic abscess apparently developed as a sequel to focal infection elsewhere in the body. From infected teeth, tonsils, sinuses or elsewhere, infection metastasized through the blood stream to the prostate gland, producing a severe prostatitis; subsequently occlusion of the ducts draining that lobe or area of the gland occurred, and finally cavitation. Once the process has started the recurrent occlusion of a prostatic duct by granulation tissue, perhaps beginning to organize, or by thick inspissated pus, leads rapidly to further dilatation of the infected pocket and hence more deformity. This etiologic theory seems fully justified in consideration of the history volunteered by many of the patients.

SYMPTOMS

It seems particularly striking that a high percentage of the cases included in this series had known of the existence of infection in the prostate for many years. Practically all of them had been treated off and on for periods varying from several to twenty years or more. Their disease was regarded simply as chronic diffuse prostatitis, and furthermore they usually noted improvement after treatment by any of the standard methods.

In many cases there were systemic manifestations of the prostatic focus of infection. Arthritis, synovitis, spondylitis, myalgic or neuromuscular pains, and neuritis such as sciatica, iritis, and torticol-

lis are only a few of the clinical entities suffered by a number of the patients.

Perhaps the most important from the standpoint of diagnosis are the local symptoms. In the majority of cases the patient will note recurrent perineal aches or pains which sometimes interfere with or prevent a comfortable sitting posture. A feeling of tension within the perineum which is improved by prostatic massage was frequently noted. Chronic urethral discharge, at times only a persistent so-called "morning drop," was prevalent in the group. An occasional patient noted marked pain or pressure referred to the base of the penis or rectum, and sometimes in these cases urination was hindered until a large amount of pus drained spontaneously from the urethra, following which a period of comparative comfort was experienced. Several of the patients stated that massage of the prostate by their local physician would result in the expression of several drams of frank pus, following which for many days or several weeks they would be free of symptoms.

In spite of these suggestive histories, in only rare instances was urethroscopic examination ever attempted, and if performed it was done hastily without any anesthetic.

DIAGNOSIS

The condition must be suspected in any case regarded as one of chronic prostatitis which fails to respond quickly to ordinary methods of treatment. A significant lead is obtained if by ordinary rectal pressure one can express an unusually large amount of pus from the gland. Sometimes a definite depression can be palpated in the gland after such manipulation. In the majority of cases urethroscopic examination is necessary for diagnosis and it should be done under the comfort of adequate anesthesia. If necessary, the hypersensitive patient should be anesthetized by inhalation or intravenous methods. A urethroscope of small caliber is preferable, as pressure from introduction of one of large size may express all the collected pus from the cavity within the prostate, thus depriving the searching eye of one of the cardinal

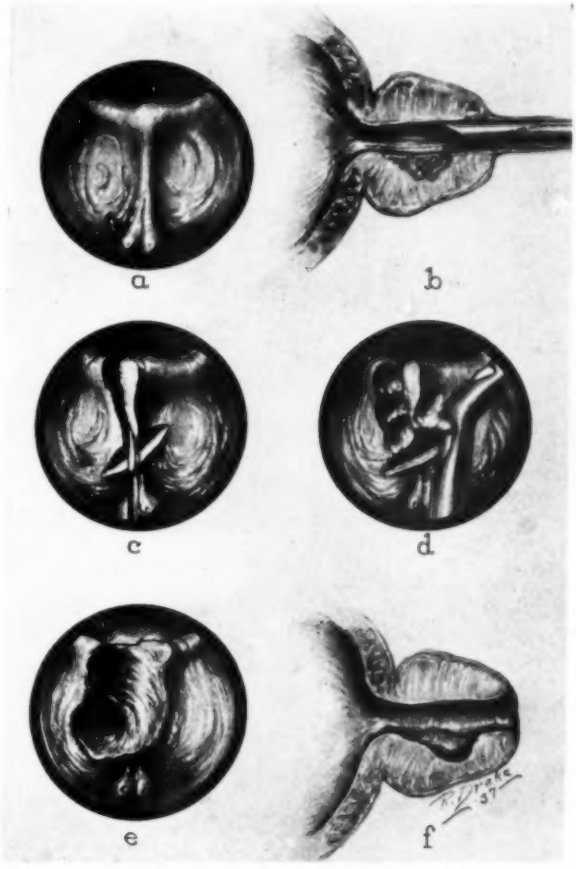

Fig. 1. a, Urethroscopic view of dilated prostatic duct; a whale bone probe is about to enter it. b, Lateral view showing relation of duct to the chronic abscess cavity; the whalebone probe has entered the cavity. c, Incision exposing cavity connected with a second incision through posterior vesical lip. d, Removal of overhanging edges with the knife punch. e, Urethroscopic view of trough through abscess cavity. f, Lateral view of completed operation.

signs of the condition. If a chronic abscess is present one can usually see without difficulty one or many dilated prostatic ducts which, as a result of ordinary pressure with the end of the instrument against the gland, will discharge a thick inspissated ribbon of pus, or if the collection be more fluid the duct will seemingly expectorate a quantity of dirty purulent material into the visual field. Counter pressure on the prostate by a finger in the rectum may be needed to force out the content of a deeply seated abscess. If by any chance the

examination is made shortly after the cavity has been emptied by massage, it may be impossible to cause a discharge of purulent material. In such cases a small whalebone probe can be employed to search a suspected duct; if a cavity is present the probe will enter without unusual force, often for a distance of several centimeters. (Figs. 1A and 1B.)

It is sometimes, though not always, possible to visualize the pocket by making a urethrogram. Various media have been employed for this purpose, one of the best solutions being a mixture of 40 per cent hippuran and tragacanth paste; campiodol is also quite satisfactory. The patient should lie partially on his side with the under leg sharply flexed toward the abdomen and the upper leg hyper-extended. By directing the rays through the pelvis at a 45° angle the femurs can be avoided and a better picture of the urethra will be

FIG. 2. Urethrogram revealing several abscess cavities in the prostate gland.

FIG. 3. Urethrogram revealing a multilocular prostatic abscess.

FIG. 4A. Prostatic calculi pre-operative roentgenogram.

FIG. 4B. Post-operative roentgenogram; all of the calculi have been removed.

obtained. The urethra should be filled with the solution and a roentgenogram made by standard technique. (Figs. 2 and 3.) The prostate should be massaged gently prior to injection, endeavoring to express from the cavity the pus which might prevent entrance of the opaque medium. If preferred an attempt can be made to fill the cavity by injecting medium through a ureteral catheter under direct urethroscopic observation. A very soft lead catheter can sometimes be coiled in the pocket, making possible an excellent roentgenographic demonstration. However, in many cases it is not possible to make a satisfactory roentgenogram even though a definite abscess cavity is present. The urethroscopic examination including if necessary probing the suspected area is by all odds the best method of diagnosis.

TREATMENT

The cardinal principle involved is promotion of drainage of the infected pocket. In order to be effective drainage must be permanent, hence obliteration of the cavity is the only solution of the problem. Each duct from which purulent material exudes must be opened widely with the electrotome. (Fig. 1C.) It is best to slice open the pocket with an incision directed toward but not through the posterior vesical lip, for if one carries it on through in one incision the knife may slip and cause injury to the anterior bladder wall. A better method is to cut down with a second incision through the vesical lip until connection is made with the first incision. (Fig. 1C.) Following this, any ragged edges overhanging the cavity are excised with a small punch or resectoscope. (Fig. 1D.) The object of all this is to make a groove through which urine will flow at each urination and flush the infected cavity in the prostate. (Fig. 1E and 1F.)

In some cases the first incision into the dilated prostatic duct opens up a cavity within the prostate into which other ducts drain. These in turn should be opened by making more incisions into them, thus going deeply into the gland. Finally a large cavity lined with numerous trabeculae resembling those seen in the bladder will be found. In some cases I have encountered cavities of at least one ounce capacity. Following thorough drainage in this manner, urethroscopy months later has shown the cavities obliterated, leaving only a scarred depression in the floor of the prostatic urethra.

Calculi are found in the infected pockets in a fair proportion of cases. These can be easily exposed and flipped with the knife edge into the bladder, from which they are removed with a large cystoscope. I have found in several cases more than 100 calculi varying in size from less than a millimeter to more than one centimeter in diameter. In rare instances it has been necessary after delivering large stones from an infected pocket into the bladder to introduce a lithotrite and crush the stones before the fragments were small enough to be withdrawn through the cystoscope. (Figs. 4A and 4B.)

After all the cavities have been carefully opened and the overhanging edges have been trimmed away bleeding is carefully controlled by electrocoagulation. A catheter is then inserted to be left in place for twenty-four hours. By that time the urine should be free from blood and the catheter has served its purpose. Regular urination is then desirable so that the saucerized cavities can be freely flushed during the process of healing.

Prostatic massage should be avoided for several weeks; by then the incised area should be healed.

RESULTS

After six or eight weeks it is wise to study the prostatic secretion carefully to note whether or not there has been a reduction in the degree of prostatitis. In the large majority of cases the secretion will contain much less pus and in many will be comparatively normal. In this series 80 per cent of cases noted immediate improvement in symptoms.

In the majority it has been impossible to re-examine the prostate gland six months or more after operation. However, the results in those cases which have returned for examination have been excellent.

CONCLUSIONS

1. Chronic prostatic abscess is not infrequently the underlying cause of persistent infection in cases regarded simply as chronic diffuse prostatitis.

2. In such cases urethroscopic examination will usually disclose dilated prostatic ducts which incompletely drain cavities which lie deep within the gland; sometimes these can be demonstrated by urethrography.

3. The cavities should be obliterated by incision with the electrotome and excision of overhanging tissue with a resectoscope; prostatic calculi which are found should be removed.

4. Elimination of the prostatic infection can be accomplished in the large majority of such cases.

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Tumors of the bladder are undoubtedly quite rare below the age of thirty years. Küster reports them most frequently between the ages of thirty and sixty years. . . . Papillomata occur as multiple tumors more frequently than any other neoplasm.

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THE DIAGNOSIS AND MANAGEMENT OF HYDRONEPHROSIS SECONDARY TO URETEROPELVIC OBSTRUCTION OF THE NONCALCULOUS TYPE

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THE problem of ureteropelvic obstruction of the noncalculous type has aroused increasing interest in the past decade. Trendelenberg, Kuster, and Fenger were the pioneers in the conservative treatment of hydronephrosis, according to Walters,[1] and the contributions of Bazey, Albarran, and others added greatly to the knowledge of the problem. The percentage of failures remained relatively high, estimated by Mathe and de la Pena[2] at 22 to 33 per cent. The important contributions of Peck,[3] Schwyzer,[4] and von Lichtenberg,[5] stimulated a renaissance of interest, the impetus of which was greatly increased by a series of successful cases reported by Quinby[6] in 1927, Walters and Braasch[7] in 1929, and others. Limited space prohibits a detailed description of improvements mentioned by these observers. Suffice it to say that the percentage of failures has steadily diminished and if one follows closely certain fundamental principles derived from the accumulated knowledge of those who have reported end results after an extensive experience, good results may be expected in the conservative treatment of hydronephrosis, if sufficient functioning tissue remains. Until comparatively recently, nephrectomy was the operation of choice in this group of cases. In 1935, Henline[8] reported sixty-six cases requiring surgical treatment in which there were forty-five nephrectomies, fourteen nephropexies with or without division of aberrant vessels or constricting bands, and six plastic operations involving the ureteropelvic juncture. Although his series of cases began in 1923, most of the conservative operations had been performed within the last few years and nephrectomy seemed the operation of choice until 1930. This coincides with my own experience, a review of which reveals that prior to 1930 there were ten nephrectomies and no plastic operations for hydronephrosis of the noncalculous type. Since then there have been eleven plastic operations on ten patients, in one of whom the condition was bilateral, and seven nephrectomies which were necessary because of advanced destruction of the renal parenchyma. It is my feeling now that prior to 1930, nephrectomy was performed in a number of cases in which the involved kidney might have been spared if present-day conservative measures had been instituted

SPECIAL CONSIDERATIONS

The diagnosis of hydronephrosis of moderate or large proportions is fairly simple and depends upon the demonstration of an abnormal amount of urinary retention in the involved organ. In the earliest stages occasionally it is difficult to differentiate from a normal kidney having a naturally large pelvis. As pointed out by Braasch,[9] the determination of the emptying time, which normally should not exceed fifteen minutes, may suffice to identify an early hydronephrosis. Henline[10] recently studied the emptying time of the kidney in relation to the fluid intake and demonstrated that marked delay may occur in the presence of slow excretion after the restriction of fluids. The diagnostic importance of the delayed film is well illustrated by Case X, Figure 11. After fifteen minutes much of the media was retained in the renal pelvis and none was visualized along

the ureter. A diagnosis of early hydronephrosis was made and a plastic operation advised but was refused. After six months the patient returned for treatment when 127 c.c. was aspirated as compared with 16 c.c. at the original examination. It should be kept in mind that a negative urinalysis and negative original roentgenogram do not exclude the disease. Braasch[9] advises that every patient with pain in either upper lateral abdominal quadrant should be subjected to urographic or cystoscopic examination if the pain is not typical of some abdominal lesion.

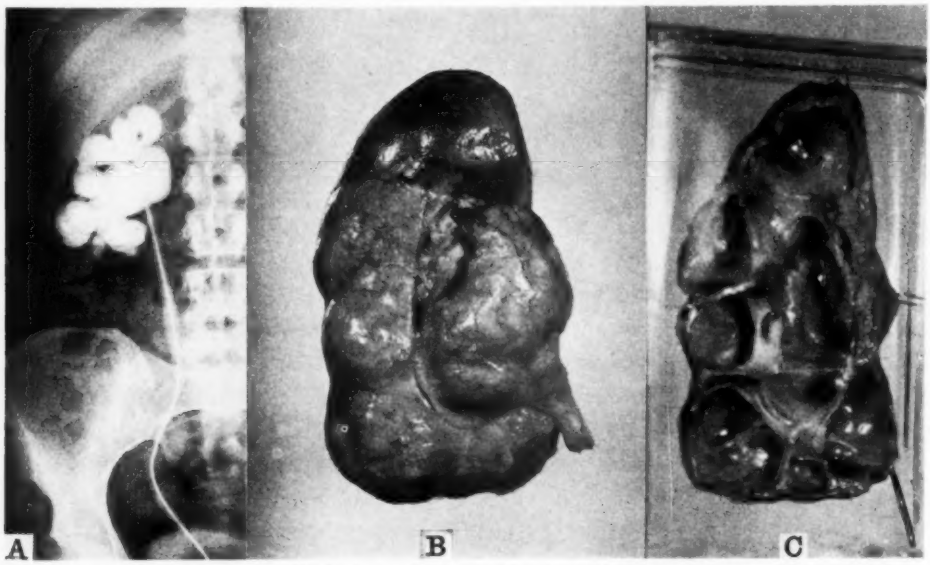

Fig. 1. A, right pyelogram disclosing a hydronephrosis of intrarenal type, with evidence of obstruction at ureteropelvic juncture. B, note that the ureter apparently leaves the pelvis at its most dependent point but that in C the ureteral opening is located high on the anterior aspect of the renal pelvis, forming a valvular type of obstruction.

Hydronephrosis may be demonstrated clearly by excretory urography if the function is not too greatly impaired, but it can not be relied upon to indicate the site or type of obstruction. Its routine use often will indicate some evidence of hydronephrosis in the opposite kidney, as recently pointed out by Sargent.[12] Widely dilated calices and pelvis may be visualized in the urogram in the presence of an obstruction in the lower ureter; however, the dilated upper portion of the ureter might not be apparent because of failure of the media to become sufficiently admixed with the retained urine above the obstructed point. If the site of the obstruction is not clearly disclosed by the urogram retrograde pyelography should be employed, preferably with serial films. In this portrays a well-filled hydronephrotic sac, constant absence of the media in the upper ureter may indicate an obstruction at the renal outlet.

Having diagnosed a noncalculous obstruction at the ureteropelvic juncture, its character usually remains obscure until the surgical exploration. Even then it may be recognized with difficulty unless the ureteropelvic region is clearly exposed and visualized before the kidney is delivered into the incision, as emphasized by Henline.[8] Occasionally even direct inspection at the time of operation fails to disclose the obstructive factor. In such cases it is advisable to open the renal pelvis and visualize the ureteral orifice which may be found at a much higher point than is indicated by the external appearance. This is well illustrated by Figure 1. In this case the ureter apparently left the renal pelvis at its most dependent point, but on opening the pelvis it was observed that the ureteral orifice was fully 2.5 cm. above this point. In hydronephrosis of the adynamic

type, a plastic or conservative operation should not be attempted if the opposite kidney is sound.

Obstructions may be due to intrinsic or extrinsic causes, more frequently the latter. The various types of obstruction found at operation were as follows: (1) Aberrant vessels were found in fifteen cases and was the most common type of obstruction. It is possible that such vessels acquire an abnormal relationship to the ureter as the individual develops, as they are of frequent occurrence in the presence of hydronephrosis in adults and are seldom found in children. From a study of 4,903 postmortem examinations of children, Bugbee and Wollstein[13] did not find a single instance of aberrant vessels, although there were many cases of hydronephrosis among them. The exact mechanism by which an aberrant vessel produces a hydronephrotic change is not clear. Quinby[14] has suggested that a pulsating vessel in contact with the ureter may interfere with normal peristalsis. On this assumption one would expect obstruction to occur frequently at the point where the ureter crosses either the terminal portion of the common iliac vessels or the beginning of the external iliac vessels; this is a very uncommon site, however, for obstructions to exist. Neither does this theory explain those cases where only an aberrant vein is found, which of course does not pulsate. A more plausible theory possibly is based on abnormal renal mobility. In the erect posture and during the normal excursions of the kidney during respiration the frequent impingements of the organ over an unyielding vessel may eventually lead to dilatation of the pelvis, accompanied by increase in weight and finally to angulation of the ureter with actual mechanical obstruction. This view is compatible with the finding of hydronephrosis associated with aberrant vessels in the third and fourth decades of life. The average age in this group of twenty-seven patients was 37.3 years. The youngest was 9 years of age and the eldest 72. (2) Lateral insertion of the ureter with the formation of a valvular type of obstruction is of common occurrence and was found eight times in this series. If interference with

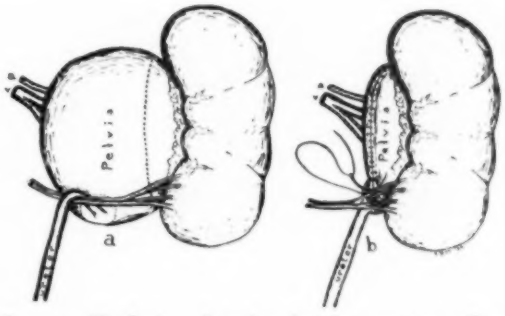

Fig. 2. Technic of re-implanting ureter after resection of a large hydronephrotic sac; a "cuff" of pelvic tissue is preserved affording more accurate approximation of mucous membrane to mucous membrane, a lessened tendency to subsequent cicatricial stenosis, and less disturbance of the physiological motility of the structures.

adequate pelvic drainage occurs, pyelectasis ensues; the larger the sac becomes, the more compression is exerted on the ureter; the stasis predisposes to infection with the production of peripelvic adhesions commonly observed with this type of obstruction. (3) Stricture at the ureteropelvic juncture is an occasional cause; it is easily confused with local spasm. McKay,[15] in 1931, reported a case of congenital hypertrophic ureteropelvic obstruction in which there was a tremendous hypertrophy of the circular muscular layer, also a condition not to be confused with stricture. (4) Periureteral connective tissue produces an angulation and narrowing of the lumen. Walters[16] mentions this as a common cause. It was found only once in this series, however. (5) Segmental atony of the ureter has been demonstrated experimentally by Beach[17] as a cause of hydronephrosis and was probably a factor in one of this series. (Case III.)

RENAL FUNCTION

If the dye tests of renal function are interpreted in the usual way they may lead one into error. Failure of indigo carmine to appear at the ureteral orifice of the affected side within thirty minutes after its intra-

venous injection does not necessarily denote absence of function. It may have been excreted in a normal amount and degree reasonable time, it may be assumed that the function is hopelessly impaired and nephrectomy is indicated.

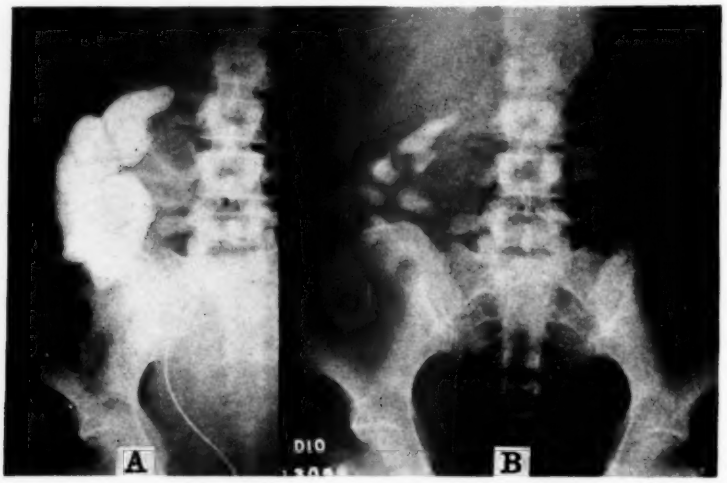

FIG. 3. (Case I.) A, retrograde pyelogram of congenital solitary kidney; 240 c.c. retention. B, excretory urogram obtained five years and three months following lateral anastomosis of the renal pelvis and upper ureter.

and have accumulated in the dilated renal pelvis. If phenolsulphonphthalein is used, with a ureteral catheter properly in place, the appearance of the dye may be delayed and only a trace be found within the normal time limits unless the specimen is collected after first emptying the sac. In all cases an effort should be made to bring out reserve function if the original tests indicate absence of function. This is accomplished by leaving the catheter in place for continuous drainage for several days and repeating the test. In a recent case, in which there was a right hydronephrosis of 270 c.c. capacity, there was no return of phenolsulphonphthalein from the emptied sac thirty minutes after the intravenous injection. The catheter was left in situ and nine days later the dye appeared after four minutes; 10 per cent was excreted the first thirty minutes. The same kidney three months following a conservative plastic operation began to excrete the dye after two and one-half minutes with an output of 10 per cent in fifteen minutes (Case VIII). It should be emphasized that if reserve function can not be demonstrated after a

TREATMENT

Conservative surgical treatment of hynephrosis may be (a) of necessity where a solitary kidney is involved, where there is bilateral involvement, or where removal of the opposite kidney is necessary, as for example in Case VI; (b) by choice, if the opposite kidney is in a healthy state. In this series a plastic operation was considered a necessity in three cases: one a solitary kidney, another in which the opposite kidney harbored a malignant neoplasm requiring nephrectomy, and in a third case there was bilateral involvement. Conservation of the organ was by choice in seven, the opposite organ having been proved of sound condition.

In a review of seventy-one cases in which conservative operations were performed, Walters[18] reported that fifteen (21.12 per cent) required secondary nephrectomy. Judging from his experience in this comparatively large group of cases, one is confronted with the prospects of failure in one case in five. This calls for a nicety of judgment in the selection of cases, especially when the operation is of choice.

In reaching a decision between nephrectomy and conservative operation, Walters has stated the following principles: (1) a conservative operation should not be attempted. (3) Although small aberrant vessels may be divided with impunity, it is

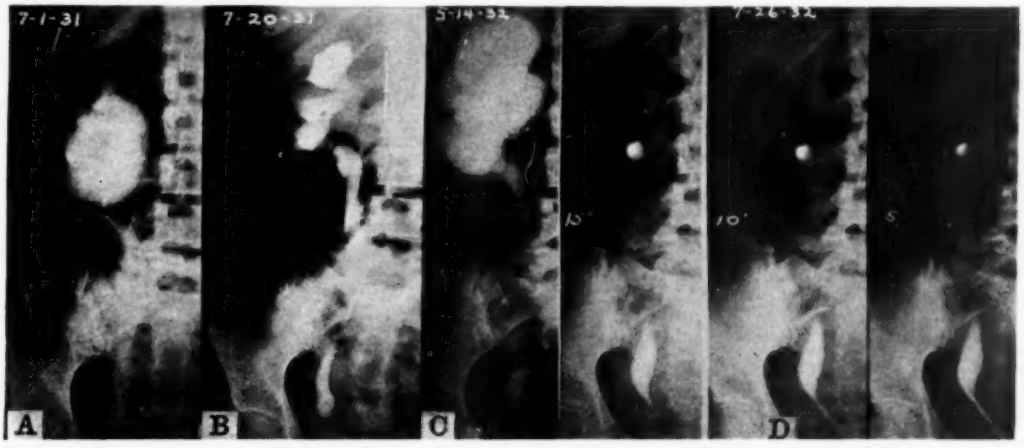

Fig. 4. (Case III.) A, retrograde pyelogram; 205 c.c. retention. B, pyelogram obtained fourteen days following ureteropyeloneostomy with resection of sac; ureteral atony. C, ten months later, recurrence of hydronephrosis; secondary nephrectomy. D, serial ureterograms made two weeks after nephrectomy; ureteral atony persists; the radiopaque media is retained after fifteeen minutes.

a conservative operation in children should receive serious consideration because of the long life expectancy with the possibility of some accident to the other kidney; (2) in women during the child-bearing period functioning renal tissue should be preserved because of the additional strain thrown upon the excretory apparatus by pregnancy and also because of the dilatation of the ureters and renal pelves during pregnancy, with the ever-present possibility of infection of the previously normal side; (3) in men whose greatest requirement is ability to work regularly, nephrectomy will be the operation of election in many cases; (4) in both sexes after middle life, nephrectomy will offer the simplest and surest method of treatment, and the probability of injury or damage to the other kidney is correspondingly less.

If conservative surgical treatment is contemplated, the following principles should be considered and observed: (1) The surgeon must be prepared to recognize and completely abolish the type of obstruction found at operation. (2) If the function is hopelessly impaired and reserve function can not be induced by continuous drainage, better to remove the ureter from a large aberrant vessel, either by resecting the pelvis in such a manner that the reconstruction will draw the ureter away from the vessel, as advocated by Young,[19] or by severing the ureter and reimplanting it. (4) If the sac is large, its resection is desirable rather than plication because of the prompt elimination of the element of stasis which enhances the relief of infection. (5) Lateral insertion of the ureter is usually amenable to a lateral anastomosis of the ureter with the renal pelvis. This operation has proved most satisfactory in five cases in which it was used. Foley[20] has recently reported excellent results in a series of cases of this type in which his modification of the Schwyzer "Y" operation was employed. (6) The Heineke-Mikulicz type of plastic, as originally advocated by Fenger, is often unsuccessful because of stricture formation or a buckling of the ureter on the opposite wall to the line of suture, as recently demonstrated by Herbst and Polkey[21] in a series of animal experiments. (7) In the presence of subepithelial fibrosis or congenital hypertrophic obstruction, the Ramstedt type of operation, as advocated by

Davis [22] and later by Vose,[23] has been used successfully. (8) Splinting of the ureter is desirable, either by the pre-operative insertion of a ureteral catheter or by passing such a catheter down the ureter a short distance with the other end emerging from the incision through a nephrostomy tube. (9) A temporary nephrostomy is an advantage as suggested by von Lichtenberg.[5] The tube should not be removed until evidences of active infection have subsided. Ormond[24] has emphasized the necessity of carefully analyzing those cases in which a conservative operation has met with failure and has called attention to the advisability of leaving the splinting catheter in place for several weeks instead of the usual five to ten days. In the cases of his series in which he had to perform a second operation, he attributed his satisfactory results to this measure. Cabot[25] has pointed out that contraction of scar is one of the chief causes of complete failure and that the prevention of this by maintaining the required position for a period of about three months in all types of plastic surgery may be considered almost a law. He suggests that the splinting catheter be left in place at least two, or perhaps three, months with the view of overcoming the serious danger of contraction at the site of the operation. (10) Infection usually can not be eliminated before the operation because of stasis. It should be treated by drainage and the sac filled with an antiseptic solution, such as neutral acriflavine (1:1000) immediately before the operation. Infection does not seem to affect adversely the success of the operation, as mentioned by Quinby,[6] provided proper aseptic and antiseptic precautions are observed. (11) Every effort should be made to eradicate the infection following the operation. In stubborn infections the ketogenic diet, mandelic acid therapy, and sulfanilamide have proved of great value. (12) Nephropexy is indicated in those cases in which ptosis is a feature; in some cases in which a small aberrant vessel or constricting band is divided, nephropexy may be all that is necessary for relief of the obstruction. In this series it seemed advisable in seven of eleven plastic operations.

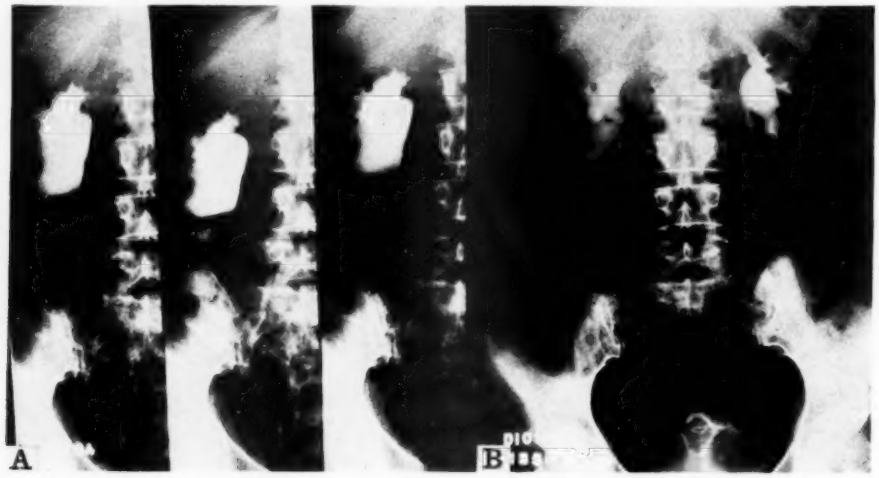

Fig. 5. (Case iv.) A, serial pyelograms; 42 c.c. retention; note constant absence of media in upper ureter, indicating an obstruction at the ureteropelvic juncture. B, excretory urogram made six months following ureterpyeloneostomy with resection of sac.

Although Quinby,[6] Walters,[18] and Henline[8] have advocated severance of the ureter and reimplantation at a site well removed from an aberrant vessel, the animal experimentation of Alksne[26] indicates that transverse section of the ureter may seriously interfere with ureteral peristalsis, causing recurrence of hydronephrosis. This possibly occurred in one of my cases which required a secondary nephrectomy one year later (Case iii). Walters has emphasized the necessity of accurately

suturing mucous membrane to mucous membrane in reimplanting the ureter. In two recent cases in which the capacity of the sac was quite large (270 c.c. and 303 c.c. respectively) the resection could not be properly effected without complete severance of the ureter. It was conceivable that a narrow cuff of the renal pelvis could be preserved at the upper end of the ureter, affording a wider circle for reattachment and more accurate approximation at the most dependent point of the reconstructed pelvis. At the same time the pelvo-ureteral neuromuscular mechanism would be less likely to be disturbed. This type of reimplantation was easily accomplished (Fig. 2). Recently it was discovered that this is essentially Delbet's type of ureteropyeloplasty and a very similar technic was employed with good results in one of six cases reported by Smith,[27] in 1931. The results of this operation have been very gratifying; the pre-operative and postoperative pyelograms obtained in both cases are presented (Figs. 8 and 9). It is evident that there has been no interference with ureteral peristalsis. After four months only 26 c.c. retention was found as compared to 270 c.c. before operation in one case and in the other one 22 c.c. was aspirated after seven months, as compared to 303 c.c. before operation. (Cases VIII and IX.)

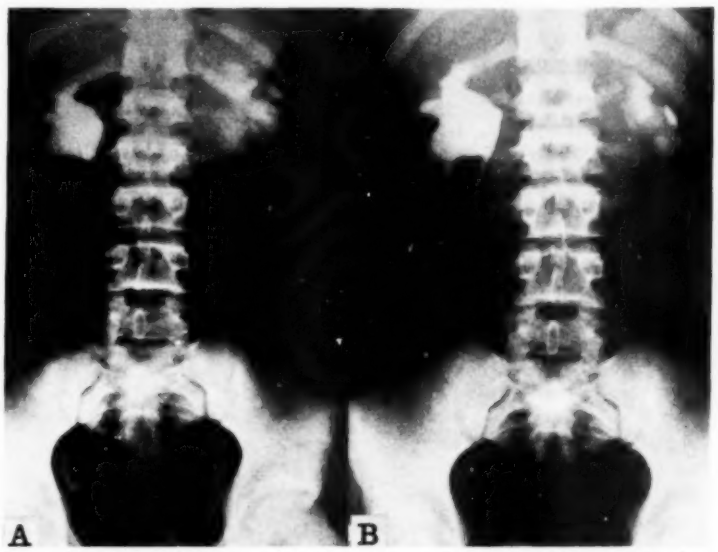

Fig. 6. (Case V.) A, excretory urogram disclosing bilateral hydronephrosis and marked impairment of function of the left kidney. B, urogram obtained one year following a right nephropexy and division of a fibrous band at the ureteropelvic juncture; and a lateral anastomosis, with resection of the sac, on the left kidney.

REPORT OF CASES

Case 1. A woman, aged 25, had suffered occasional attacks of pain in the right loin, associated with rigors and fever, since early childhood. On physical examination there was a large, rounded, tender mass in the right loin. The temperature was 104. On cystoscopic examination 240 c.c. of turbid urine was aspirated from the right kidney. There was no evidence of a left ureteral orifice. Excretory urography disclosed only the hydronephrotic right kidney. No media appeared in the left renal area. There was no return of indigo carmine after thirty minutes. On October 2, 1930, exploration of the congenital solitary kidney revealed a high lateral insertion of the ureter, producing a valvular type of obstruction. The upper 4 cm. of the ureter was anastomosed laterally to the distended renal pelvis. The sac was not resected; a No. 11F ureteral catheter was left in place for drainage; she was discharged on the twenty-second day with the incision completely healed. After three months the capacity of the renal pelvis was 58 c.c.; after six months, 23 c.c. Phenolsulphonphthalein returned in three minutes; 23 per cent was excreted in fifteen min-

utes; no infection; seven years later still enjoying excellent health. An excretory urogram January 30, 1936, disclosed good function and no evidence of a recurrence of hydronephrosis. (Fig. 3.)

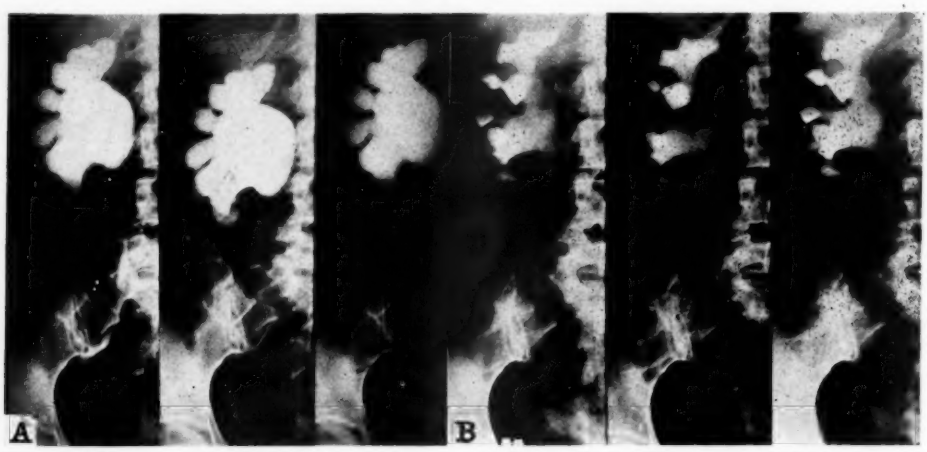

Fig. 7. (Case vi.) A, serial right pyelograms; note constant absence of media in upper ureter indicating high obstruction; 75 c.c. retention. B, postoperative serial pyelograms, obtained six months following a lateral anastomosis of the renal pelvis and upper ureter.

Case ii. A woman, aged 47, complained of dull pain in the right loin, associated with frequency of urination beginning two years before. On examination 66 c.c. of turbid urine was aspirated from the right renal pelvis. Indigo carmine appeared after five minutes from the left ureteral orifice and ten minutes from the right with faint concentration from the right. Serial right pyelograms disclosed marked extrarenal dilatation of the pelvis and constant absence of the media in the upper ureter. Exploration of the right kidney revealed a large artery and vein at each pole of the kidney. There were no vessels at the hilus. The sac was resected to within 1 cm. of the renal substance with preservation of a v-shaped segment which was stitched into the divided upper ureter at the point of contact with the large anomalous vessels; nephropexy drawing the vessels further away from the ureter; nephrostomy. Postoperative course marked by much abdominal distention and adynamic ileus. On the eleventh day there was great distention of the colon, spontaneous perforation, peritonitis, and death on the twelfth day. Autopsy revealed plastic repair of the kidney in perfect condition. Postmortem pyelogram was essentially normal. There was no evidence that the fatal intestinal lesion was directly related to the operation upon the kidney.

Case iii. A woman, aged 35, had complained of pain in the right upper abdominal quadrant, fever and urinary frequency, beginning three years before. Examination disclosed an infected right hydronephrosis of 205 c.c. capacity; function impaired about 25 per cent. The ureter was diffusely dilated and atonic, terminating as a narrow point in the intramural portion. The upper ureter was redundant and markedly narrowed at the junction with the large dilated pelvis; left kidney normal. July 6, 1931, sac resected; redundant, strictured upper ureter resected; pelvis reconstructed and ureter implanted at most dependent point; nephrostomy. On the fourteenth day, only 18 c.c. of urine aspirated from renal pelvis. Pyelogram disclosed satisfactory immediate result although the entire ureter was diffusely dilated below point of anastomosis. Gradual recurrence of hydronephrosis and atony of ureter persisted in spite of dilatations and a ureteral meatotomy. (Fig. 4.) One year later a secondary right nephrectomy was performed; one month later serial ureterograms showed a persistence of the atonic ureter which did not empty after fifteen minutes; symptomless.

Case iv. A woman, aged 54, first noticed hematuria seven months before with aching pain in the right loin; recurrence of hematuria four days before; 42 c.c. of urine aspirated from right kidney; grossly infected. Phenolsulphonphthalein appeared after four minutes from the left, seven minutes from the right, with 10 per cent from the left and 8 per cent from the right in fifteen minutes. Serial right

pyelograms revealed an extrarenal type of hydronephrosis with evidence of obstruction at the ureteropelvic juncture. At operation, pelvis (Fig. 5). Phenolsulphonphthalein appeared after three minutes from the right, two minutes from the left, with an output of 17 per

Fig. 8. (Case VII.) A, plain roentgenogram; note group of numerous small shadows in left renal area. B, excretory urogram; the shadows are included in the dilated left renal pelvis, which is evidently obstructed at the ureteropelvic juncture. C, serial retrograde pyelograms obtained twenty months following a lateral anastomosis with resection of sac and removal of the numerous small stones; note diminished capacity and evidence of normal ureteral peristalsis.

August 7, 1934, lateral insertion of the ureter found. Sac resected, ureter severed, and reimplanted at most dependent point. No. 9 ureteral catheter, passed from below, left in place; temporary nephrostomy; nephropexy. Twenty months later condition excellent, no further symptoms, right pyelogram essentially normal, although mild degree of infection persisted; 15 c.c. of urine aspirated from right cent from the right, and 22 per cent from the left in fifteen minutes.

Case V. A boy, aged 16, complained of pain in the left loin, associated with rigors and fever, beginning five years before. From early infancy until he was eleven years of age he had had occasional rigors and fever, unaccompanied by pain. Elsewhere he had been given fifteen or twenty cystoscopic treatments without benefit.

Examination disclosed bilateral hydronephrosis. There was approximately 40 c.c. retention on the right and 128 c.c. retention on the left. Indigo carmine failed to return after fifteen minutes from either side; 75 c.c. of cloudy urine was aspirated from the right kidney and 3 c.c.

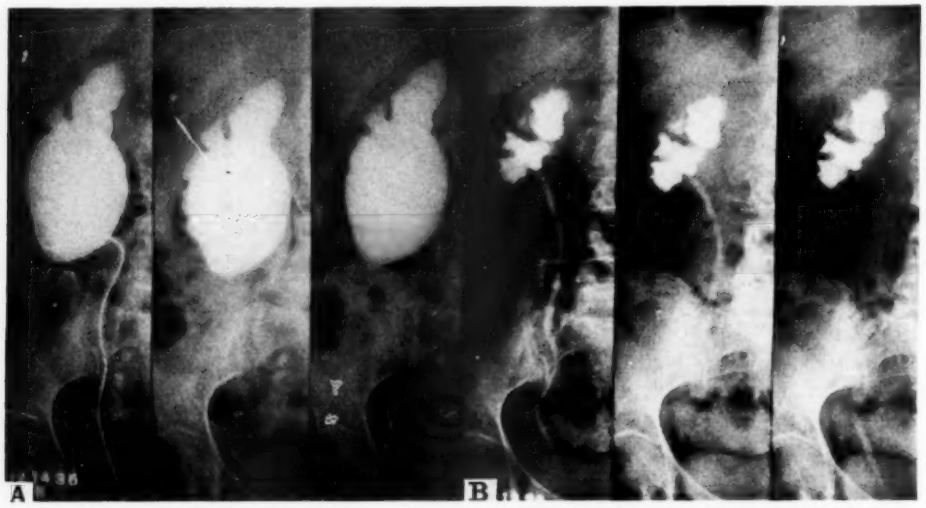

Fig. 9. (Case VIII.) A, serial right pyelograms; evidence of obstruction at the ureteropelvic juncture; 270 c.c. retention. B, postoperative series of pyelograms made seven months following resection of sac and reimplantation of ureter, employing the technic illustrated by Figure 2; note evidence of normal ureteral peristalsis and rapid emptying.

The urine from the left kidney was grossly infected with escherichia coli. Phenolsulphonphthalein appeared after five minutes from both sides with an output of 5 per cent from the right and 5 per cent from the left, in fifteen minutes. July 28, 1934, the right kidney was explored and a fibrotic band divided where it crossed the ureter at its juncture with the pelvis; nephropexy; four weeks later the left kidney was exposed and a lateral anastomosis performed for a valvular type of obstruction, due to lateral insertion of the ureter. The sac was resected; temporary nephrostomy. Discharged on the sixteenth day; incision completely healed. Three months later 58 c.c. aspirated from left renal pelvis; twelve months after operation excretory urogram revealed pelvis and calices on the left approaching normal in outline and good function. Capacity of the right pelvis was essentially unchanged (Fig. 6). Twenty-one months later the patient was enjoying good health. In this case the infection rapidly cleared under a ketogenic diet.

Case VI. A woman, aged 30, complained of pain in the left loin, associated with hematuria beginning eleven months before. There was moderate tenderness in the left loin, moderate anemia and loss of weight. Examination revealed cloudy urine from the right ureteral orifice and hemorrhagic spurts from the left. from the left; phenolsulphonphthalein returned after twelve minutes from the right and six minutes from the left with an output of 22 per cent from the right and 2 per cent from the left in thirty minutes. Pyelography disclosed a right hydronephrosis, with evidence of an obstruction at the ureteropelvic juncture, and the characteristic deformity of a cortical neoplasm involving the left kidney. January 14, 1935, the right kidney was explored; there was a high and lateral insertion of the ureter for which a lateral anastomosis was made; the sac was not resected; a ureteral catheter was left in place; temporary nephrostomy and nephropexy. Following a smooth convalescence, on February 7, 1935, a left nephrectomy was performed because of a carcinoma occupying the middle third of the kidney. Six weeks after the right ureteropyeloplasty, 45 c.c. of urine was aspirated from the right kidney. Phenolsulphonphthalein appeared after three minutes with 15 per cent excreted in fifteen minutes; fifteen months later she was enjoying good health, there was no evidence of a recurrence of the malignancy, and the right kidney was in satisfactory condition. (Fig. 7.)

Case VII. A woman, aged 59, complained of attacks of severe pain in the left loin which began one year before. The original roentgenogram revealed a group of numerous, closely

set, small shadows in the left renal area. There was no history of the patient having passed stones. An excretory urogram identified the shadows as those of numerous small stones almost filling the left renal pelvis which was moderately dilated; there was evidence of good function. The right kidney was of normal outline and function. Apparently there was an obstruction at the ureteropelvic juncture on the left side which had not permitted any of the small, shot-like stones to pass. Exploration on October 9, 1935, revealed a high insertion of the ureter for which a lateral anastomosis was performed. The sac was resected and the stones removed. A catheter was passed down the ureter as a splint, the upper end being brought out of the incision through a nephrostomy tube. She was discharged from the hospital November 6, 1935, the incision had healed and there was no further pain. Approximately twenty months later phenolsulphonphthalein appeared after two and one-half minutes from the right kidney and three minutes from the left, with an output of 22 per cent from the right and 9 per cent from the left in fifteen minutes. The left renal specimen contained an average of one pus cell per high power field and an occasional colon bacillus. She was symptomatically well and the left pyelogram approached normal outline. There was no evidence of recurrence of stones nor abnormal retention of urine (Fig. 8).

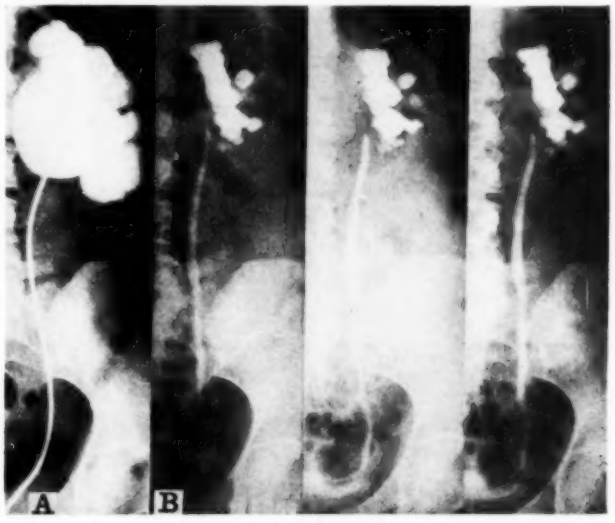

Fig. 10. (Case IX.) A, retrograde pyelogram; 303 c.c. retention. B, postoperative pyelograms obtained seven months later; note markedly diminished capacity and normal ureteral peristalsis.

Case VIII. A woman, aged 57, complained of pain in the right loin which began six years before, associated with a palpable mass at times in the right upper abdominal quadrant. On examination, December 7, 1935, 270 c.c. of cloudy urine was aspirated from the right renal pelvis. Phenolsulphonphthalein appeared after four minutes from the left kidney and failed to appear from the right during thirty minutes of observation. Serial right pyelograms disclosed a constant absence of media in the upper ureter. A catheter was left in place for continuous drainage; five days later phenolsulphonphthalein appeared after ten minutes from the right side with an output of 5 per cent in thirty minutes. December tenth the appearance time was four minutes and 10 per cent was excreted in thirty minutes. At the same time the left kidney excreted 30 per cent. Having thus demonstrated reserve function the kidney was explored December 20th. The ureter was acutely angulated over a small vein at the lower pole. The large sac was resected and a narrow cuff of renal pelvis was left intact about the upper ureter which was accurately sutured at the most dependent point of the reconstructed pelvis. The ureteral catheter was left in place and a temporary nephrostomy was performed. Convalescence was very satisfactory and she was discharged from the hospital on the eighteenth day. Seven months later reexamination revealed 9 c.c. of retention which

was free of pus, but there were many B. coli. Phenolsulphonphthalein appeared after three and one-half minutes from the right and after two and one-half minutes from the left; during a fifteen-minute period 8 per cent was excreted from the right and 13 per cent from the left. Right serial pyelograms disclosed the pelvis and calices of almost normal outline and there was normal ureteral peristalsis (Fig. 9).

Case IX. A woman, aged 38, was examined April 23, 1936, because of attacks of severe pain in the left loin which had their onset in early childhood. The attacks lasted from three to seven days. Four years before a plain

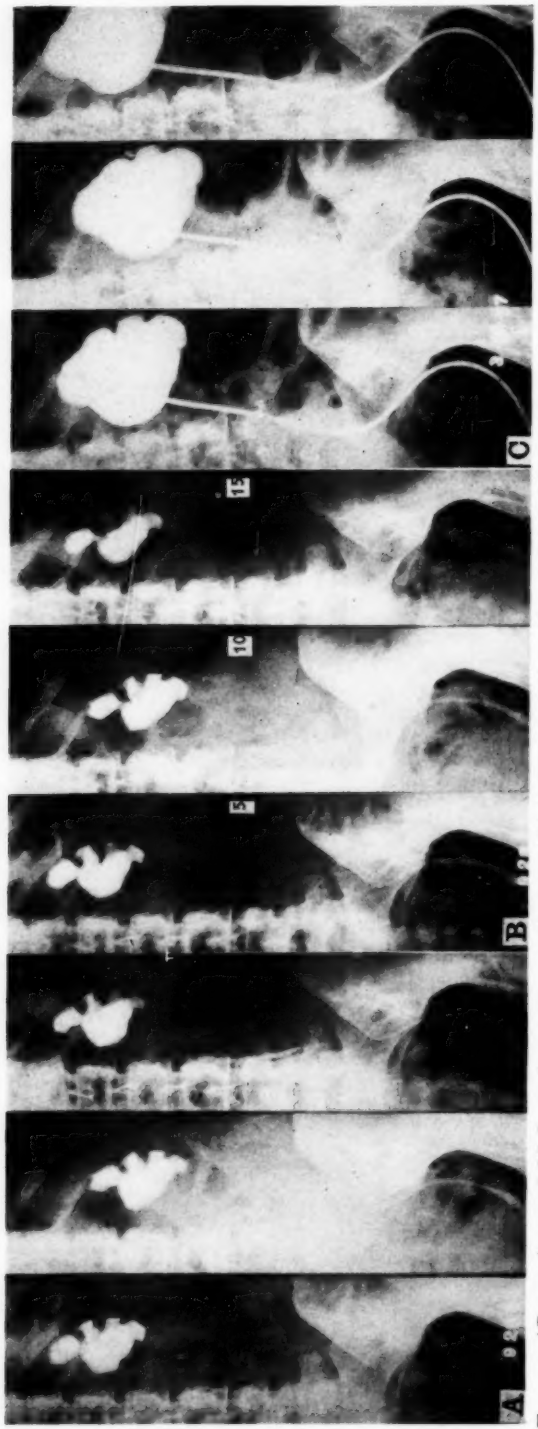

Fig. 11. (Case x.) A, serial left pyelograms revealing a mild degree of pyelectasis. B, serial delayed films disclosing retention of media five, ten, and fifteen minutes after retrograde injection. Note constant absence of media in upper ureter, indicating an obstructive factor at the ureteropelvic juncture. Treatment refused. C, pyelogram of same kidney six months later, proving correctness of original diagnosis and the value of determining the emptying time in early hydronephrosis.

roentgenogram and urinalysis made elsewhere had been reported negative, with exclusion of a urological lesion. The left kidney was palpably enlarged. An excretory urogram revealed the right kidney of normal function and outline. No media appeared in the left renal area. On cystoscopic examination there was absence of urinary excretion from the left orifice; 303 c.c. of clear urine was aspirated from the left renal pelvis; the pyelogram gave evidence of an obstruction at the ureteropelvic juncture. At the operation the following day a small aberrant artery and vein were found at the lower pole, causing compression and angulation of the ureter. Resection of the sac was performed with preservation of a narrow cuff of renal pelvis attached to the ureter and reimplantation at the most dependent point. A No. 9F ureteral catheter was left in place and a temporary nephrostomy was done. The ureteral catheter was removed on the eighth day and the nephrostomy tube on the twelfth day. After seven months she was symptomatically well. On cystoscopic examination only 22 c.c. could be aspirated from the left kidney. The specimen contained an average of four pus cells per high power field and a few bacilli of the colon type. Phenolsulphonphthalein appeared after four minutes from the right, six minutes from the left, and 46 per cent was excreted from the right and 7 per cent from the left in fifteen minutes. Serial left pyelograms disclosed a moderate degree of retention but a remarkable reduction in the total capacity as compared with the original pyelograms. (Fig. 10.) Fifteen months later she reported that her health was excellent and that there had been no indication of a return of the former symptoms.

Case x. A woman, aged 41, was examined September 24, 1936, because of attacks of severe pain in the left loin which began three years before. The attacks had averaged about one each week for the previous five months; usually had lasted about twenty-four hours, occasionally forty-eight hours, and required an opiate for relief. Pain radiated from the left lumbar region to the left abdomen and occasionally to the thigh. On cystoscopic examination, indigo carmine appeared after seven minutes from the left and after three minutes from the right. There was no obstruction to ureteral catheters and 5 c.c. was aspirated from the right renal pelvis and 16 c.c. from the left. Serial left pyelograms revealed evidence of an obstruction at the ureteropelvic juncture with retention of much of the media after fifteen minutes. (Fig. 11.) Under the diagnosis of an early hydronephrosis and obstruction at the ureteropelvic juncture, exploration of the kidney was advised but refused. Six months later she returned for attention, the attacks having become increasingly severe and more frequent. There was a palpable, tender mass deep in the left loin. On cystoscopic examination 127 c.c. of urine was aspirated from the left renal pelvis. Phenolsulphonphthalein appeared after three minutes from the right and after six minutes from the left, with an output of 42 per cent from the right and 3 per cent from the left during thirty minutes. Serial pyelograms were repeated, disclosing a large hydronephrosis. The following day the kidney was explored. An aberrant artery and vein crossed to the lower pole over which the distended pelvis folded, combined with a marked angulation of the ureter. Compression of the vessels with rubber-covered forceps produced no apparent change in color and they were divided with removal of about 1 cm. of their substance. There was also evidence of a valvular type of obstruction as the ureter emerged from the pelvis about 2 cm. from the most dependent point. The ureter was densely adherent to the pelvis over this distance, being bound by a rather dense sheath of fibrous tissue. A lateral anastomosis of the von Lichtenberg type was performed, combined with a temporary nephrostomy and a No. 9 catheter as a splint, which had been inserted from below prior to the operation. Her convalescence was uneventful and the ureteral catheter was removed on the eighth day, the nephrostomy tube on the tenth day, and she was dismissed from the hospital on the seventeenth day, at which time the wound was completely healed. The urine still contained pus, graded 11. The pyuria persisted in spite of all measures and repeated pelvic lavage. After three months no function could be demonstrated from the left kidney which contained about 34 c.c. of thick pus, accompanied by moderate fever and local tenderness in the left loin. Approximately three months following the plastic operation, a secondary nephrectomy was performed. The region of the anastomosis was a mass of dense, cicatricial tissue which evidently was the cause of persistent obstruction. Had the splinting catheter been left in place over a longer period,

as suggested by Ormond and by Cabot, it is believed the outcome of the plastic operation might have been successful. Her convalescence following the nephrectomy was uneventful.

SUMMARY

1. Of a series of twenty-seven cases of ureteropelvic obstruction of the noncalculous type, requiring surgical treatment, there were eight males and nineteen females. The average age of the group was 37.3 years. The right kidney was involved in sixteen, the left in ten, and in one the condition was bilateral. Aberrant vessels were found in fifteen, lateral insertion of the ureter in seven, fibrous bands in two, and in three the exact nature of the obstruction was indeterminate. Prior to 1930 nephrectomy was the operation of choice and was performed ten times; since 1930 eleven conservative plastic operations have been done, of necessity or by choice, on ten patients with satisfactory results in seven; in one a secondary nephrectomy was necessary one year later; and three months later in another; one death occurred at the end of the second week from an intestinal lesion. Since 1930 only seven primary nephrectomies have been performed for hydronephrosis, the function having undergone hopeless impairment.

2. In those cases subjected to plastic operations the pre-operative pyelographic and functional data are submitted, and also the end results.

3. Points in diagnosis are discussed with special reference to urography, serial pyelography, and the unreliability of the dye tests for renal function, as usually obtained. In instances without demonstrable function at the original examination an effort should be made to bring out reserve function by continuous ureteral catheter drainage.

4. The more important principles to be observed in the surgical treatment of hydronephrosis are stated.

5. In cases requiring severance and reimplantation of the ureter, the advantages of preserving a flange of tissue from the pelvis are mentioned (Delbet type of ureteropyeloplasty): affords a more accurate anastomosis; less chance of subsequent cicatricial stenosis; and minimal disturbance of the pelvo-ureteral neuromuscular mechanism. The method is especially adaptable to large hydronephroses requiring resection of the sac and in cases in which a large aberrant vessel cannot be divided safely. Continuity of the ureter, however, should be preserved whenever possible in all cases.

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It is usually noted that bladder tumors, except in comparatively rare instances, remain well confined to the bladder cavity and do not tend to invade surrounding structures; nevertheless, metastases to distant points are not infrequent.

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MANAGEMENT OF THE PREVESICAL SPACE*

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SUPRA-PUBIC section of the urinary bladder represents the oldest urologic operation. It is the most common emergency procedure in the field of urinary tract surgery. Despite its constant use the operation is often performed in a haphazard and not infrequently a careless manner. This is evidenced by a mortality rate out of all proportion to the gravity and complexity of the procedure. Familiarity engenders indifference to a point where sound surgical principles are too often neglected. Despairing of asepsis the surgeon too often forgets the alternative of antisepsis and contaminates the cystotomy wound which might otherwise be kept clean.

The value of a dependable technique for section of the urinary bladder is obvious. It is a procedure which many general surgeons are called upon to undertake. To the urologist, the operation is so routine that too frequently it is relegated to juniors with the intimation that it is too ordinary for serious consideration. Too often this attitude lowers the surgical standard and increases the mortality record of a procedure which should be relatively benign.

This operation has come down to us from a legendary background. Two standardized methods of approach have been developed, both of which possess merit. The verticle or median incision is the older and by far the more common. The alternative is the transverse technique. The latter has its advantages in fat individuals where postoperative hernia is suspicioned. Both methods are described in textbooks of surgery and urology.

During cystotomy two complications confront the surgeon. The first is the inadvertant tearing of the peritoneum. The second is the spread of infection to the prevesical space. The axiom that the weakest link determines the limits of any procedure is applicable to surgery. In cystotomy, contamination of the prevesical space is certainly the weakest link. Any refinement which adds to the strength of this link should be considered.

Distention of the bladder, whenever practical, preparatory to cystotomy has been in common practice since its introduction by the versatile anatomist Rossitus (circa 1580). The solution used has varied with the years. Sterilizing agents are the present vogue. Young and Davis advocate 1 per cent meroxyl.[5] This has a higher sterilizing coeficient than boric acid solution but is slightly more irritating to the bladder. It is common practice to open the bladder and drain off the solution by suction. The introduction of a catheter to which is attached a length of rubber tubing sufficient to reach to the floor will allow the bladder to be filled by gravity. The tube may then be clamped off and the end placed in a receptacle beneath the table. When unclamped the bladder will be emptied by the siphoning action of the tube. This eliminates a great deal of spilling of infected bladder content into the wound.

Following exposure of the bladder, the prevesical fascia must be separated in order that the anterior fold of the peritoneum may be reflected upward. A finger wrapped in gauze can be used for this but often results in separation of the bladder from the prevesical space. Lateral dissection as advocated by Cabot[1] may be used, or the bladder can be steadied by the opposite hand while reflecting the peritoneal fold.

Management of the prevesical space should be an important step in any cystot-

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omy. The prevesical space is filled with loose fat, delicate areolar tissue and a rich blood supply derived from the plexus of Santorini's. It is an ideal soil for infection pelvic cellulitis and even thrombo-phlibitis. Anatomically it can be dependently drained only through the perineum. It is in such close proximity to the pubic arch that infection has not infrequently been transmitted beneath the periosteum resulting in involvement of the bony structure. Pelvic cellulitis is the predominent cause of deaths following cystotomy. In spite of this, surgeons go on year after year opening this area to contamination. The large tubes so frequently placed in this space often serve to keep the wound freshly supplied with infected urine which falls by gravity through or about the tube.

In 1913, the late Granville MacGowan advocated surgical closure of the prevesical space during the operation.[4] This important contribution seems to have escaped general usage. Keyes advocates much the same procedure in his description of cystotomy by a two stage method.[3]

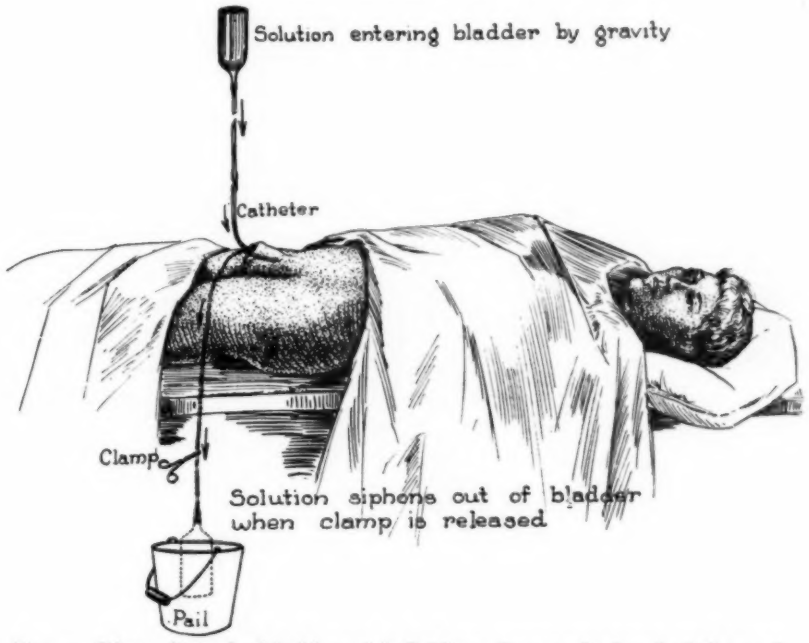

Fig. 1. Distending the bladder with fluid to elevate the level of the peritoneum. When emptied, the same tubing will act as a siphon to drain the bladder.

To close the prevesical space, a suture of No. 2 chromic catgut mounted on a round curved needle is introduced at the lowest angle of the wound. From above downward, the needle passes through: one, the sheath of the rectus muscle, two, the fibres of the rectus muscle, three, into (but not through) the musculature of the bladder thence upward through, four, the fibres of the opposite rectus muscle and finally out through the, five, sheath of the rectus muscle. This is illustrated by Figure No. 2.

The suture is now tied securely and the prevesical space is thus permanently closed. When done before the bladder is opened, this important area can be kept surgically clean.

The tubing connected with the catheter is now opened and the bladder is emptied by siphoning off the accumulated urine which has been sterilized by the antiseptic solution previously injected to inflate the bladder. Incision can now be made into the bladder by a stab opening and enlarged either by a transverse or median incision.

Following the contemplated procedure, closure of the bladder may be done either with or without supra-pubic drainage. In general it is prudent to drain the bladder. The position of the tube should be as near as possible to the site of the attachment of the urachus.

The occlusion stitch closing the prevesical space will generally care for this area. Where drainage is felt necessary, the use of a capillary rubber strip in place of the usual stiff tube is advocated. Such a drain was described by the author in 1929, in which the capillary action of two opposed surfaces of rubber tissue is utilized to drain a deep space.[2]

In closing the bladder, the mucosa may be approximated by a purse string suture of No. 1 plain catgut about the cystotomy tube or self retaining catheter. The bladder musculature is best closed with interrupted sutures of No. 2 chromic cat gut. The recti muscles are approximated by loosely placed sutures of No. 1 plain cat gut. The topmost suture is passed superficially through the bladder musculature in order to block off permanently the peritoneum from the dome of the bladder. This admits of a rapid approach to the bladder in the event that subsequent cystotomy becomes necessary. Careful approximation of the subcutaneous tissue will go far to hasten the healing of the wound. The skin may be closed by a subcuticular stitch, by clips or by sutures.

These procedures are applicable both to cystotomy for drainage and cases where

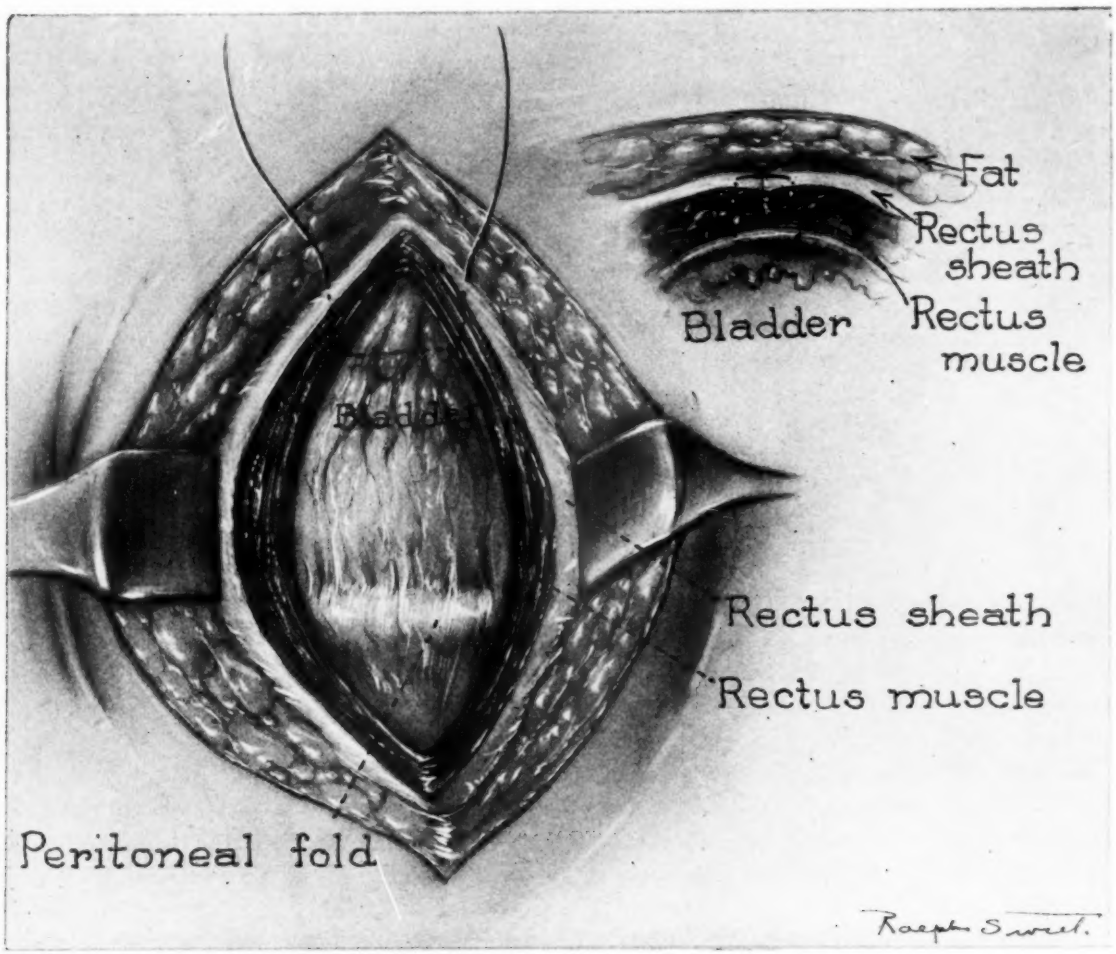

Fig. 2. Introduction of the suture to close off the space of Retzius.

operative procedures are contemplated. Attention to those simple refinements will strengthen the weak links in this important operation and thereby materially lower its hazard.

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Longitudinal wounds of the ureter heal quickly and require the simplest sort of repair.

. . . . . .

From our knowledge gained by work on dilatation of ureteral strictures it is probable that a catheter of large calibre would find its way by the injured area more readily than one of small size.

From—"Modern Urology" Edited by Hugh Cabot, M.D., C.M.G., F.A.C.S.

THE TREATMENT OF THE URINARY BLADDER IN CASES WITH INJURY OF THE SPINAL CORD*

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INTRODUCTION

THE most common cause of death exclusive of the first week after injury in patients with spinal cord injuries is unquestionably some kind of systemic infection. Certainly 75 per cent[1] or more of these infections originate in the genito-urinary tract. This condition has been recognized for a long time and many attempts have been made to deal with it. Older therapy has included constant and intermittent catheter drainage, total absence of any bladder drainage and suprapubic cystostomy. End-results have been measured in shibboleths, the most popular of which has been the "automatic bladder." In addition there has been widespread ignorance of the normal activity of the bladder as well as of the changes that result when its nervous connections with the brain were broken. Ignorance of the particular and peculiar side effects produced on all reflex activity of any type of spinal cord injury is also widespread. It should be obvious that treatment of the urinary bladder in patients with spinal cord injuries, regardless of the details of the method, can only be carried out and can only prove satisfactory when the surgeon bases it on a knowledge of the following fundamental data: (1) the normal functional physiology of the bladder, (2) the peculiarities of spinal cord injuries and (3) the changes in bladder function that follow injury to the spinal cord or cauda equina.

THE NORMAL PHYSIOLOGY OF THE URINARY BLADDER

A detailed exposition of this can not be attempted here. Denny-Brown and Robertson[2] have covered it and their papers should be consulted by anyone who desires more than a superficial knowledge of this matter. Contradictory work from other sources is negatived for the most part because of the failure to take into account either the effect of spinal shock[3] or the necessity for carrying out measurements by means of a rate of fill,[4,5] that approximates the physiologic.

In brief it is now apparent that the normal bladder empties in response to a reflex stimulation. (Fig. 1.) This reflex is initiated by some degree of stretching of the bladder wall. This varies with and is peculiar to the individual, and is produced by the cubic content of urine present in the bladder. This reflex emptying can be inhibited but can not be initiated except by failure to inhibit. Owing to the type of muscle in the bladder wall, the organ fills by alternate stretch and contraction. The basic tonus which is present during the stretch period gradually increases with successive contractions. If not inhibited, any one of these contractions may reach a level which will empty the contents of the bladder provided a certain basic minimum amount of fluid is present. If inhibition is complete such emptying contractions may remain absent until the normal bladder has become so distended as to stretch the musculature beyond the possibility of any contracture, (Fig. 1B) or it may be terminated by a series of tetanic spasmodic contractions. (Fig. 1A.) Voluntary interruption of bladder emptying even during the outflow of urine can be accomplished by contraction of the external sphincter or cut-off muscle. Ordinary inhibitory impulses arise out of the effect of posture, the

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environment, or unfavorable psychological influences.

The reflex emptying contraction that arises out of the stretch of the bladder wall is appreciated by the individual as urgency. As this stretch increases, the urgency becomes more extreme until it eventually ceases to be urgency and becomes pain. The non-emptying contraction waves that alternate with the periods of relaxation of the detrusor muscle can also be made to reach emptying levels, regardless of the amount of bladder content. This can be accomplished, however, only when the individual is able voluntarily to relax his external sphincter and simultaneously compress the fundus of the bladder by an increase of intra-abdominal pressure.

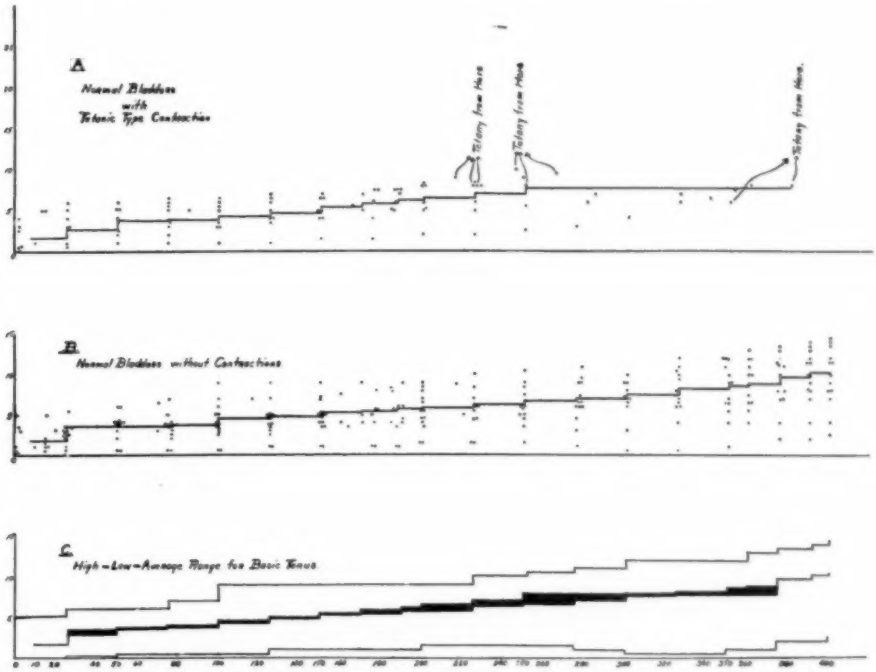

FIG. 1. Graphs of normal bladder activity. The abscissa or horizontal arm indicates amount of fill, the ordinate or vertical arm the amount of intravesical pressure.

The Segmented Neural Pathways to and from the Bladder. The bladder emptying reflex belongs to the segmental spinal reflex group. It has two complete reflex arcs. The central connections of both these arcs lie in the upper sacral spinal segments. The pathways of the first arc are formed by units of the parasympathetic or pelvic nerves. Those of the second by the pudic nerve. The pudic nerves are somatic in type and may therefore carry voluntary motor impulses in addition to those of purely segmental reflex origin. The parasympathetic nerves do not carry motor impulses that originate in the cerebral cortex as volitional responses to sensory stimuli.

The first or parasympathetic reflex motor response occurs as the result of the sensory stimulus found in the stretching of the bladder wall. It takes the form of a simultaneous contraction of the detrusor muscle and relaxation of the internal or upper end of the urethral sphincter. This simultaneous action permits urine to flow into that part of the posterior urethra that lies between the internal and external sphincters.[8] The presence of urine in this area serves as a sensory stimulus to the reflex activity subtended by the second or pudic nerve reflex arc. These sensory and motor impulses both travel by way of the one mixed nerve. The motor response of this second reflex stimulus relaxes the external sphincter from its normally contracted state. This completes the opening of the bladder outlet and permits the contents to

escape. *Voluntary inhibition* of micturition is caused by impulses originating in the cerebral cortex. They contract the external sphincter or cut-off muscle when it is in a reflexly induced state of flaccidity. *Voluntary facilitation* of micturition may conceivably be associated in part with relaxation of the normally contracted external sphincter because of impulses originating in the cerebral cortex and reaching the muscle by way of the spinal cord and pudic nerves. The pathways for the inhibitory impulses that act to prevent detrusor contraction by way of the first or parasympathetic reflex arc are not clearly understood. It is probable, however, that these impulses arise in the lower rather than the higher cerebral levels and that they prevent the completion of the reflex by acting on the central synapses in the lateral horns of the sacral cord. As was pointed out above, facilitation of detrusor contraction occurs only by virtue of failure to inhibit it.

In addition to these two reflex arcs there are other less well understood neurologic connections. One is in the nature of a third reflex mechanism. It lies completely within the substance of the bladder wall and is analagous to Auerbach's plexus in the intestinal musculature. It acts only when the bladder is completely disconnected from the spinal cord, whether physiologically or anatomically, and in the absence of spinal shock. Through it the detrusor is caused to contract weakly and the internal sphincter to open simultaneously and briefly. Since the external sphincter has been necessarily denervated at the same time that the bladder was, it is constantly flaccid and urine is therefore permitted to flow from the bladder during the weak detrusor contraction. The sensory impulse that initiates this inefficient motor response is again found in the stretch of the bladder wall. Constant bladder activity that is based for any appreciable length of time on this neurologic foundation leads to detrusor hypertrophy and to marked diminution in the cubic capacity of the organ. Such a bladder may properly be spoken of as *autonomous*. Finally the bladder has a nervous connection by way of the presacral or hypogastric plexus. This is a part of the sympathetic nervous system. It is not known whether this connection serves to carry sensory impulses from the bladder or motor impulses to the bladder.[9,10] There is good evidence, however, that the sensation of pain caused by overstretching of the bladder wall is carried centrally over these pathways.[2] Opinion as to other functions must await further data.

THE PECULARITIES OF SPINAL CORD INJURIES AS THEY EFFECT BLADDER ACTIVITY

There is one accompaniment of *all* spinal cord injuries that has an important and usually completely unappreciated effect on the activity of the urinary bladder. This is *spinal shock*. The pathology of spinal shock is not known but its effects are. They can be best explained by citing its definition. Spinal shock is that condition which, when caused by spinal cord injury of any type, produces suppression or alteration of segmental reflex activity below the level of the cord injury. This change will be greatest in those segments that are next to the point of major injury and least in those segments that are furthest away. Spinal shock may be indefinitely prolonged or caused to recur after any period of absence if, in addition to the cord injury, the patient develops a major infection or becomes severely exhausted, whether from operation, pain or any other cause. Spinal shock is an invariable accompaniment of any spinal cord injury for some minimal period of time. All bladder activity depends upon the integrity of the segmental reflex arc. Obviously, therefore, such activity will be interfered with during the period of spinal shock. The interference will be most if the cord injury is low and will tend to decrease as the level of injury mounts.

In addition to spinal shock there are certain other cord injuries that peculiarly effect the activity of the bladder. A destructive lesion of all sacral segments or of the

cauda equina will anatomically denervate the bladder. No matter what type of treatment is used, the best functional classification that such a bladder can attain will only be of the autonomous variety. The wall will therefore tend to hypertrophy and the cubic capacity to decrease. Voluntary control of the contents will be permanently and completely lost. An anatomical transection at whatever level will also leave permanent changes in the bladder activity. Such a lesion interrupts all impulses from the brain. Inhibition of emptying contractions can no longer be carried out. The bladder empties itself as soon as its wall is sufficiently stretched regardless of the suitability of surroundings, the time of the last emptying or any other extraneous circumstances. Voluntary interruption of this emptying can not be accomplished either. Such a bladder is of the *uninhibited reflex* type and is the best functional end-result that can be obtained after spinal cord transection. Finally operation, cystitis, pyelitis, infected bedsores and chronic pulmonary infections may each, when added to a spinal cord injury, cause spinal shock to recur and bladder activity to regress toward the flaccid atonic minimal.

The Successive Changes in the Functional Activity of the Bladder that Follow Injury to the Spinal Cord or Cauda Equina. Regardless of the type or location of spinal cord injury, the bladder passes through certain constant phases in the course of its progress toward recovery from the atonic state to which it has been reduced by spinal shock. These are five in number. The characteristics of each group overlap those of the immediately succeeding and preceding groups to a variable degree. Furthermore the transition toward functional normality may be so rapid as to suggest that certain of the groups may not need to be included. This error is due however, to the infrequency of observation. The "cord bladder" is successively atonic, autonomous, hypertonic, of an uninhibited reflex type and the normal "cord bladder." Based on observations of normal bladders as published in earlier papers,[1,6] it is possible to classify bladder activity in accordance with certain standards. These standards are four in number. They have to do with the initial and sustained tonus of the detrusor muscle during the fill, the presence of emptying contractions and the optimum storage capacity of the bladder, as deduced from them, the absolute amount of residual urine expressed in terms of percentage of fill and the reflex activity of the external urethral sphincter.

DETRUSOR TONUS

In the normal bladder the initial tonus ranges between 0 and 5 cm. of water and the average curve of sustained tonus shows a steady rise from 2½ to 10 cm. in a fill of 400 cc. During this rise the alternate periods of relaxation and contraction are constantly equal until either the rise is terminated by an emptying contraction or the detrusor muscles goes into tetany. In accordance with these standards the *atonic* bladder has a slight decrease (1¾ cm.) in initial tonus and a slightly flatter curve of sustained tonus (rise of 5¾ instead of 7½ cm. in a fill of 400 cc.). The *autonomous* bladder has twice as high an initial tonus (5½ cm.) and a steeper curve of sustained tonus (rise of 9½ cm. in 400 cc. of fill). The *hypertonic* bladder has seven times as high an initial tonus, and a curve of sustained tonus that rises 23½ cm. in a fill of 400 cc. The *uninhibited reflex* and the normal "cord bladders," except for a slight increase in initial tonus, show no significant change from normal.

EMPTYING CONTRACTIONS AND STORAGE CAPACITY

In the normal bladder emptying contractions either singly or in the form of tetany will occur provided they are not inhibited. If inhibited they may be absent throughout the test filling. The optimum storage capacity of the organ is measured by the amount of fluid which can be introduced at a physiological rate of fill up to the time of the first emptying contraction. The *atonic*

bladder never shows any emptying contractions and its storage capacity is limited only by the amount that its wall will stretch and its sphincter retain. The *autonomous* bladder shows absent or inefficient emptying contractions. The storage capacity was over 300 cc. in 76 per cent of the bladders that were studied. The *hypertonic* bladder always shows emptying contractions and the storage capacity was below 300 cc. in slightly more than half of the cases that were studied. The *uninhibited reflex* and the *normal* "cord bladder" both show the presence of emptying contractions in every case and have a decreased storage capacity (200 cc. or less in 90 per cent of the cases studied.)

ABSOLUTE RESIDUAL URINE

In the normal bladder there is no residual urine. That is, once an emptying contraction has started the bladder is emptied completely and siphonage by catheterization will yield no further fluid. This may be expressed as 0 per cent of the fill. In the *atonic* bladder residual urine is present up to 82.5 per cent of the fill, in the *autonomous* bladder to 43 per cent, in the *hypertonic* bladder to 19 per cent, in the *uninhibited reflex* cord bladder to 6 per cent; and in the *normal* cord bladder up to 16 per cent.

REFLEX ACTIVITY

Reflex activity of the external urethral sphincter as measured by either the bulbocavernosus or the anal reflex (both being supplied by the pudic nerve) is invariably present in normal bladders and invariably absent in *atonic* bladders. The response varies in accordance with the type of spinal cord injury in the other bladder classifications.

CLASSIFICATION FOR TREATMENT

It must be obvious that treatment of the cord bladder, to be efficient, must vary with the type of bladder to be dealt with. A method that would be suitable for the atonic type of bladder would be obviously unsuitable for the hypertonic or the uninhibited reflex variety. Cystometric examination before treatment is therefore essential. Furthermore inasmuch as, in the progress toward complete recovery, bladder activity (as pointed out above) changes, so must treatment be changed to suit. This in its turn predicates repetition of the cystometrograms. Cystometry to be informative must approach as closely as possible to the duplication of the physiologic processes that normally fill the bladder with urine. Only in this way can artificial changes in detrusor activity and intravesical pressures be avoided. They can not be avoided if the bladder is filled with increments of fluid that are significantly larger than those normally delivered through the ureters, nor if the small amounts of fluid are added at a greater than maximum normal rate. Cystometric measurements taken after 25 or 50 c.c. of fluid have been added as one mass can not give anything like an accurate picture of the bladder activity that is actually present. It can and has been easily demonstrated that to get such data the rate of fill must not exceed 120 drops a minute.[1,2] With this end in view an appropriate cystometer[6] was devised in 1934. It has been used since as a method of determining the type of bladder activity that is present in all spinal cord injuries before and during the treatment of the urinary tract.

The Cystometer (Fig. 2).

In its essentials the cystometer consists of a large U tube with a side opening in the proximal arm. This side arm is connected with the bladder by a length of tubing attached at its distal end to an inlying catheter. To the upper end of the proximal arm of the U tube and 70 cm. above this side outlet, an air-tight "Murphy dropper" is attached to a 600 c.c. container which is graduated in 25 c.c. amounts. Above the dropper an adjustable compressor surrounds the connecting tube. This regulates the rate of flow from the container to the dropper and permits its estimation in terms of drops per minute. The optimum rate has proved to be about 120 drops per minute. The other or distal arm of the U tube is formed by 70 cm. of glass tubing of 4 mm. bore marked every one-half cm. from a zero point which is set close to the level of the bladder connecting arm. Introduced into the bladder connection is an air vent which is of the same length as the manometer together with a three-way stopcock which allows fractional emptying of the bladder.

With the patient as nearly horizontal as possible, readings are taken with the apparatus hung on a stand at such a height minute. Inasmuch as the system is air-tight and the bladder and manometer contents are in hydrostatic equilibrium, changes in

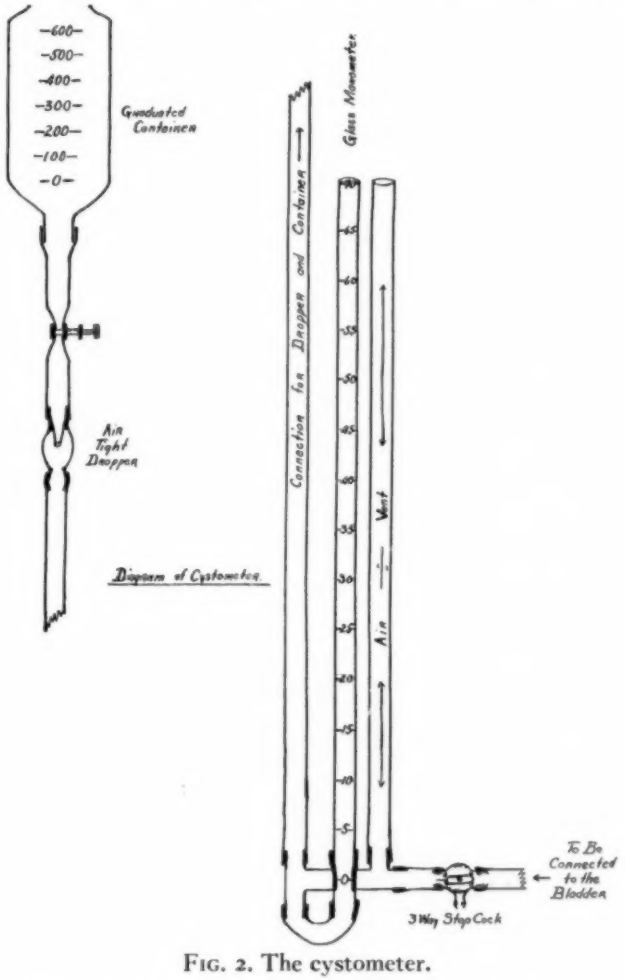

FIG. 2. The cystometer.

that the zero point on the manometer is at the level of the patient's pubis. Under aseptic precautions the patient is catheterized, the bladder emptied and the catheter fixed in the urethra with the eye just inside the internal sphincter. In males it is preferable to use a soft rubber rectal tube of appropriate size because of the terminal opening. With the catheter attached and clamped off close to the meatus the sterilized cystometer is filled to the zero point with sterile irrigating fluid from the graduated container. After making sure that the air is all out of the system the catheter is unclamped and the test filling started by adjusting the dropper so that the flow is at the rate of 120 drops per

the intravesical pressure will be registered on the manometer as rises and falls of the column of fluid contained therein. Contraction of the bladder wall or increase in this pressure will cause a rise in manometric fluid and relaxation the opposite. Respiratory excursions are visible constantly as are sudden alterations in intra-abdominal pressure when they occur. By starting the observations with the cystometer filled and the level of fluid in the container at 0 it is easily possible to make readings of intravesical pressure on the manometer scale simultaneously with notations of the amount of fluid that has emptied from the container into the bladder. These figures are recorded in parallel columns at the time

of the observation. Later, they can, if necessary, be transferred to coordinate paper in such a way as to produce a graph

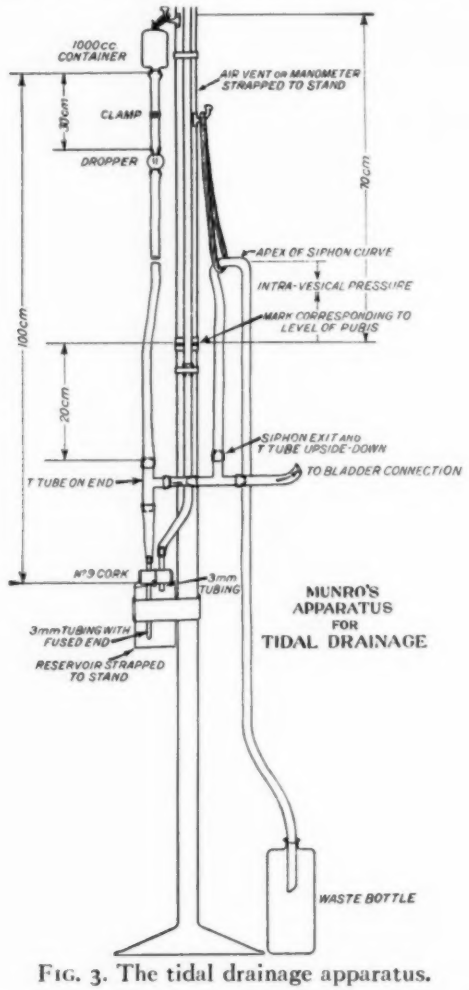

Fig. 3. The tidal drainage apparatus.

(Fig. 1) which has for its abscissa or horizontal arm the fluid content of the bladder, and for its ordinate or vertical arm the intravesical pressure at a corresponding moment. Although there is a positive inflow pressure, the slow rate and the additional safety valve effect as provided by the open ends of the manometer and air vent prevent significant artificial alteration of the measurements. The readings of pressure are isometric below 70 cm. or in accordance with the height of the air vent. In the presence of a leak about the catheter or overflow from the manometer or air vent above 70 cm. they become isotonic. Such an observation predicates the presence of an emptying contraction. When recording, each change in intravesical pressure, as evidenced by a rise or fall in the column of fluid in the manometer, is noted. The corresponding increase in bladder content as evidenced by a fall in the level of fluid in the graduated container is also listed. Care must be exercised to make the recordings in such a way as to differentiate the step rises of pressure as seen in the normal bladder and the steady rise and fall to and from a peak as seen with uncooperative patients or in completely atonic bladders.

After completing the observations detailed above, if the stopcock in the bladder connection is set at any predetermined level *above* the zero point, the full bladder may then be made to empty against positive pressure. With the stopcock *at* zero and *no further emptying*, a true picture of the residual urine in the given case may be obtained by then withdrawing by siphonage (with the stopcock *below* zero) and measuring any remaining bladder contents.

Tidal Drainage. Since 1934 I have treated the different types of "cord bladder" associated with all kinds of spinal cord injury by the so-called tidal drainage method. This was first described in association with Hahn[7] in 1935. The apparatus (Fig. 3) provides a method of filling the bladder with irrigating fluid at any predetermined rate and to any degree of intravesical pressure through an air-tight system. When the desired degree of intravesical pressure has been attained, a siphon comes into action. This siphon empties the bladder after which air is permitted to enter the system and the apparatus is automatically set up for a repetition of the cycle. The apparatus has two main parts. One is the mechanism for filling the bladder. Air is excluded from this part by a fluid seal which in turn will break after the bladder has been emptied. The other is the siphon mechanism which draws simultaneously from the bladder and the filling mechanism until both are emptied.

In setting up the apparatus the filling mechanism is put in place first. In consists of a ½ pint preserve jar which is stoppered by a #9 rubber cork. This cork has

2 perforations. Through one of these is inserted a piece of glass tubing with an inside diameter of 3 mm. one end of which is fused in such a way as to reduce the diameter of the tip to 2 mm. or less. This piece of glass tubing reaches through the cork to a point 3 mm. above the bottom of the reservoir. The outer end is joined as closely as possible by means of "stethescope" rubber tubing to one end of the horizontal arm of a glass T tube. This and the other T tube used in the siphon system *must* have everywhere an inside diameter of at least 4 mm. Openings that have been tapered to a lesser diameter must be filed off. The other end of this T tube arm is attached by way of a piece of ordinary rubber tubing 80 cm. long to the bottom of an *air-tight* glass "Murphy dropper." The upper end of this dropper is in turn attached by another piece of ordinary rubber tubing 30 cm. long to the bottom of a 1,000 c.c. container. Between the 2 is placed an adjustable compression clamp. An irrigating or other similar type of stand is now set up at the foot of the bed. On it is marked a point corresponding to the level of the patient's pubis when he is lying flat in bed. This is the "bladder level." The unused arm of the T tube is placed horizontally against the stand at a point 20 cm. below the "bladder level" and the reservoir strapped with adhesive plaster to the stand below. The 1,000 c.c. irrigator is then hung up as high up on the stand as the rubber tubing connections will permit. Through the other perforation in the #9 cork is now inserted a short piece of 3 mm. (inside diameter) glass tubing. This extends only through the thickness of the cork. It is connected as closely as possible by a length of "stethescope" tubing to a 70 cm. length of glass tubing (3 mm. bore) and this latter strapped to the irrigator stand with adhesive plaster. This part constitutes the air vent or seal.

The second portion of the apparatus or the siphon consists of a T tube used upside down together with the proper rubber tubing connections. One end of the now horizontal limb of this second T tube is attached as closely as possible through "stethescope" rubber tubing to the previously unused arm of the first T tube which is in the filling mechanism. The other end of this horizontal arm is attached to a sterile rubber *rectal tube* which has previously been properly inserted into the bladder and which is held in place by the ordinary 3-tailed adhesive plaster strapping about the penis in the male. In the female an ordinary mushroom tipped soft rubber retention catheter is used in place of the rectal tube. The attachment between the siphon T tube and the catheter is made by an appropriate length of acid-proof rubber tubing with an inside diameter of 6 mm. Any glass connections that are inserted must have an inside diameter of no less than 5 mm. at every point. Another length of this same acid-proof rubber tubing is lead upward from the remaining unused arm of the siphon T tube to some point above the bladder level where it is suspended from the stand in such a way as not to cause kinking. The distance between the bladder level and the curve of the siphon is equivalent to the intravesical pressure which will be produced by the apparatus. The amount of siphon or other tubing below the bladder level is of no importance in relation to either intravesical pressure or the operation of the apparatus. The free end of the siphon is allowed to fall downward toward the floor and to end just within the neck of a waste bottle. This free end must not, however, be permitted to get below the top of the fluid that collects in the waste bottle.

The 1,000 c.c. irrigator is now filled with 1–30,000 sterile potassium permanganate solution, and the compression clamp adjusted so that the fluid will flow into the apparatus at from 60–100 drops per minute. This flow gradually fills the preserve jar, the otherwise imprisoned air escaping by way of the air vent. With the preserve jar full, the fluid now fills all the vertical tubing and their connections up to the bladder level. From here on the irrigating fluid flows into the bladder. As the bladder is distended its increasing elastic resistance or intravesical pressure is represented by an increase in the height of the fluid levels in the tube connecting the 1,000 cc. irrigator and the preserve jar, in the air vent and in the proximal vertical limb of the siphon. Eventually, the intravesical pressure corresponds exactly to the height of the siphon curve and the fluid level in the latter is exactly at the apex of that curve. The addition of a minimal amount of fluid to the system causes this level to rise to a point where it overflows into the waste bottle by way of the distal arm of the siphon tubing. This overflow, the apparatus being now air-tight, starts a siphonage from both the bladder and the preserve jar. The bladder empties directly, the preserve jar by way of the long glass tube with the fused end and the lower two-thirds of the T tube incorporated in the filling mechanism. Because, however, of the fact that the internal diameter of the bladder outlet (5–6 cm.) is everywhere two to three times that of the narrowest point of the preserve jar outlet (2 mm. fused end), the bladder empties four times as fast as the preserve jar. The siphon is sealed against the entrance of air until the preserve jar is empty and the air vent opened. It continues, therefore, to act after the bladder is empty. As soon as the preserve jar is emptied, however, air enters by way of the air vent and stops the siphon action. This, inasmuch as the inflow still continues, permits resumption of the filling cycle

which will again be terminated by siphonage when the predetermined level of intravesical pressure is reached. The apparatus will work only if it is air-tight, and only if constructed and set up in accordance with the specifications and measurements given above. When it is working properly respiratory excursions are visible in the fluid in the air vent, the preserve jar empties completely at each cycle, and air enters only at the end of the siphonage and only by way of the air vent. Finally, if the operator expects the fluid actually to reach the bladder, the height of the siphon or intravesical pressure must be readjusted to the individual type of bladder activity whenever that changes. A completely atonic bladder can not be expected to empty if the siphon action takes place only after a high intravesical pressure has been built up. Nor can a hypertonic bladder with a high potential of intravesical pressure be expected to respond to treatment by this machine unless the siphon curve is set high enough to force fluid into the bladder in spite of its resistance. The apparatus will not function if the bladder contains large masses of detritus. They plug either the catheter or the tube in the preserve jar. Such impediments must be removed by additional hand irrigation at appropriate intervals. The catheter must be properly placed and in men *must* have a large opening on the end and not in the side. Leakage around the catheter can not be corrected by inserting bigger sizes. This will only lead to epididymitis and urethritis. Such leakage is due to an improper adjustment between the tidal drainage and the bladder it is trying to irrigate.

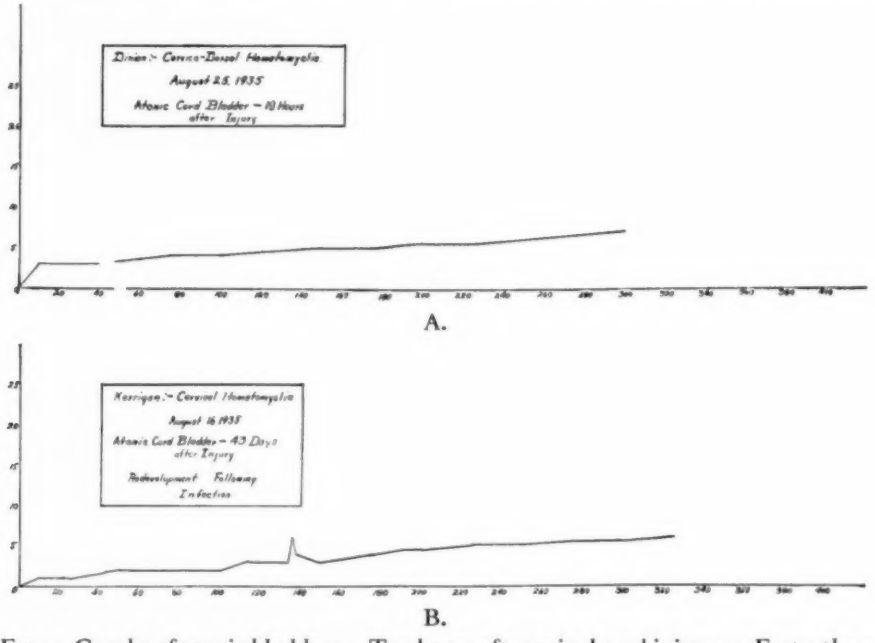

Fig. 4. Graphs of atonic bladder: A. Ten hours after spinal cord injury. B. Forty-three days after spinal cord injury and twenty-four hours after the development of an acute infection. The abscissae indicate amount of fill and the ordinates the amount of intravesical pressure.

If a bladder starts uninfected when it is attached to this apparatus it will stay so indefinitely provided certain precautions are taken. The catheter must be removed, cleaned, sterilized and replaced once a week. The entire apparatus must be disassembled, cleaned and sterilized once a week and before being used originally. The permanganate solution must be sterile and must be kept so. The open end of the 1,000 c.c. irrigator must be closed with a sterile cotton plug at all times. With these precautions, both male and female patients have been kept constantly on this appara-

tus for over eighteen months without bladder infection. These include patients both in the hospital and in their homes.

identified and treatment instituted in accordance with this finding.

Treatment of the Atonic "Cord Bladder."

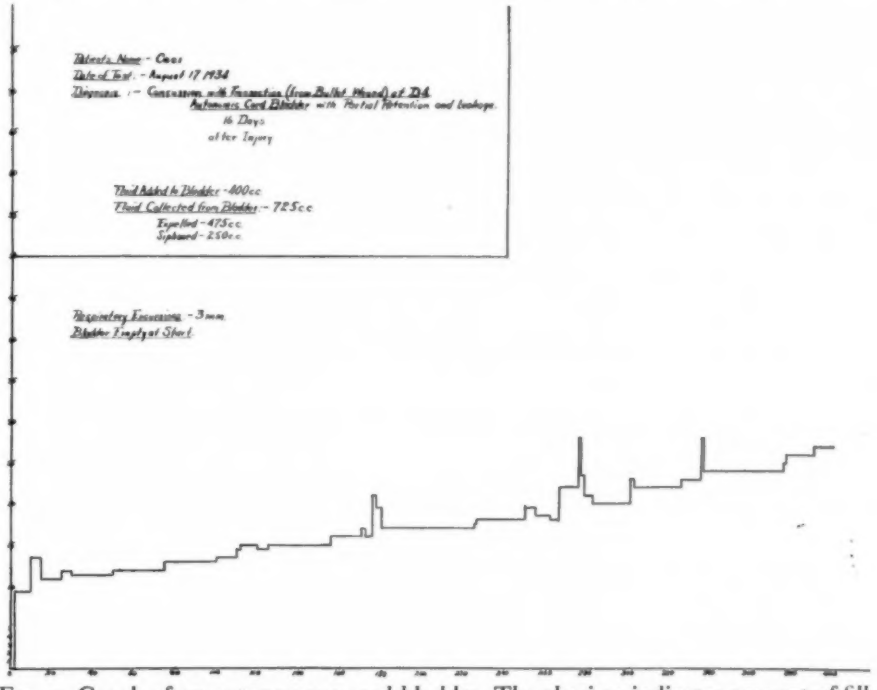
Patient's Name - Cass
Date of Test. - August 17 1934
Diagnosis :- Contusion with Laceration (from Bullet Wound) at D6
Autonomous Cord Bladder with Partial Retention and Leakage.
16 Days
after Injury
Fluid Added to Bladder - 400 cc.
Fluid Collected from Bladder :- 725 cc.
Expelled - 475 cc.
Siphoned - 250 cc.
Respiratory Excursions - 3 mm.
Bladder Empty at Start.

FIG. 5. Graph of an autonomous cord bladder. The abscissa indicates amount of fill and the ordinate amount of intravesical pressure.

Treatment of "Cord Bladders." All bladders of all spinal cord injuries that have passed through the neurosurgical service of the Boston City Hospital have been exclusively treated by tidal drainage since its development here in 1934. As soon as such patients are seen they are placed on tidal drainage without further ado. This takes precedence over all other diagnostic or therapeutic procedures except treatment for surgical shock. If instituted immediately after receipt of the injury it is presumed that the patient has an atonic bladder and the siphon level is set at 1 or 2 cm. If seen at a later date, the siphon is set at the normal figures (10–15 cm.) and efforts are made to determine whether or not the bladder is already infected. This has invariably been the case if the institution of tidal drainage has been delayed beyond forty-eight hours after the receipt of the injury and regardless of what other therapy was used. A cystometrogram is then made and the type of bladder then present

The atonic "cord bladder" (Fig. 4) is one of the accompaniments of spinal shock. It is characterized by a complete absence of emptying contractions, a low level of sustained tonus, an 80 per cent absolute residual and a spastic internal urethral sphincter. It is present in the early stages of all types of spinal cord injuries even including those with apparently complete denervation of the bladder. The symptoms are complete retention of the bladder contents. The treatment is tidal drainage at the earliest possible moment with the siphon curve or intravesical pressure set at 1 to 2 cm. or less.

Treatment of the Autonomous "Cord Bladder." As spinal shock improves or is corrected, the atonic "cord bladder" becomes an autonomous "cord bladder." (Fig. 5.) This type is characterized by inefficient detrusor contractions none of which reach the emptying levels but many of which relax the sphincters enough to permit leakage. The initial and sustained

tonus of the detrusor muscle is somewhat higher than normal. The storage capacity is increased but not to the extent reached in the atonic type and a 40 per cent absolute residual is present. The musculature gets its innervation from the intramural plexus, the segmental spinal reflex being absent. This type of bladder is present in all varieties of spinal cord injuries and is the best end-result that can be hoped for in destructive injuries of the sacral segments or cauda equina. In the acute transient cases the symptoms are those of overflow retention. In the permanent ones the symptoms are those of a greatly hypertrophied bladder with a small capacity and a complete absence of external urethral sphincteric activity. The treatment is to place the patient on tidal drainage. In the acute cases the siphon curve should be placed from 10 to 15 cm. above the bladder level. In the permanent bladders of this type, the height of the curve should be increased as much as is possible without causing leakage. Until it can be done away with, any mild chronic urinary tract infection may keep such a bladder from progressing toward cure in spite of treatment.

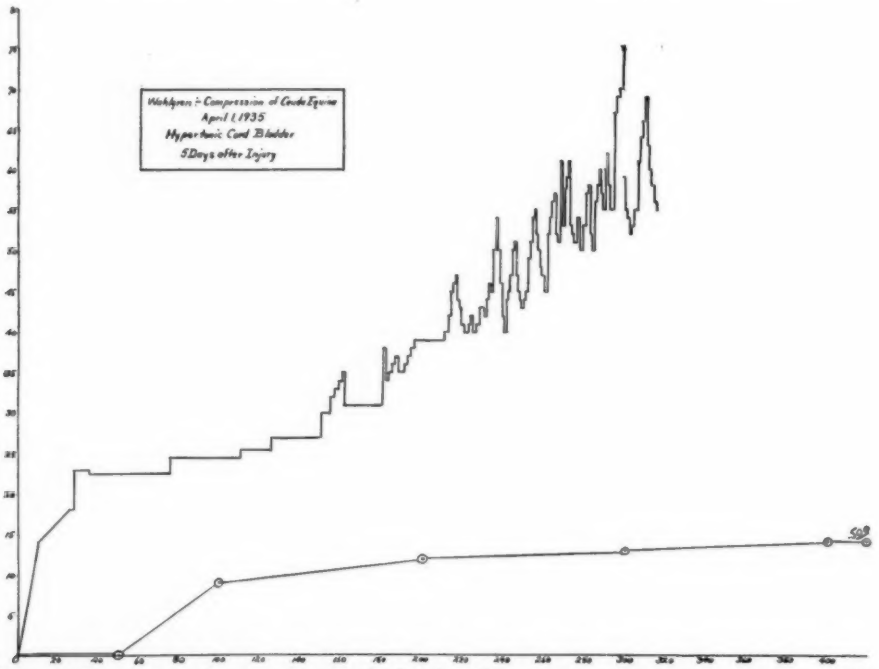

FIG. 6. Graph of a hypertonic cord bladder. The abscissa indicates amount of fill and the ordinate amount of intravesical pressure.

Treatment of the Hypertonic "Cord Bladder." If it has not constituted an end result because of the spinal cord injury autonomous "cord bladders" usually merge quickly into the hypertonic type. (Fig. 6.) In this type the initial and sustained tonus is raised to extraordinarily high levels and if not otherwise prevented the capacity will be rapidly and permanently reduced to practically nothing. Emptying contractions are stimulated by the smallest amount of contents. Even in the non-transected cord injuries there is no inhibitory control exerted. The absolute residual constitutes only 20 per cent of the fill. The activity in these bladders represents the first and completely disordered return of segmental reflex activity. Major infections, operation or any other procedure that recreates spinal shock will cause them to revert to either one of the two preceding types forthwith. Hypertonic "cord bladders" are present in all varieties of spinal injuries except the destructive lesions of the sacral segments and cauda equina. Symptoms:

they empty themselves at irregular frequent intervals and the patients are constantly wet unless they are on tidal drainage.

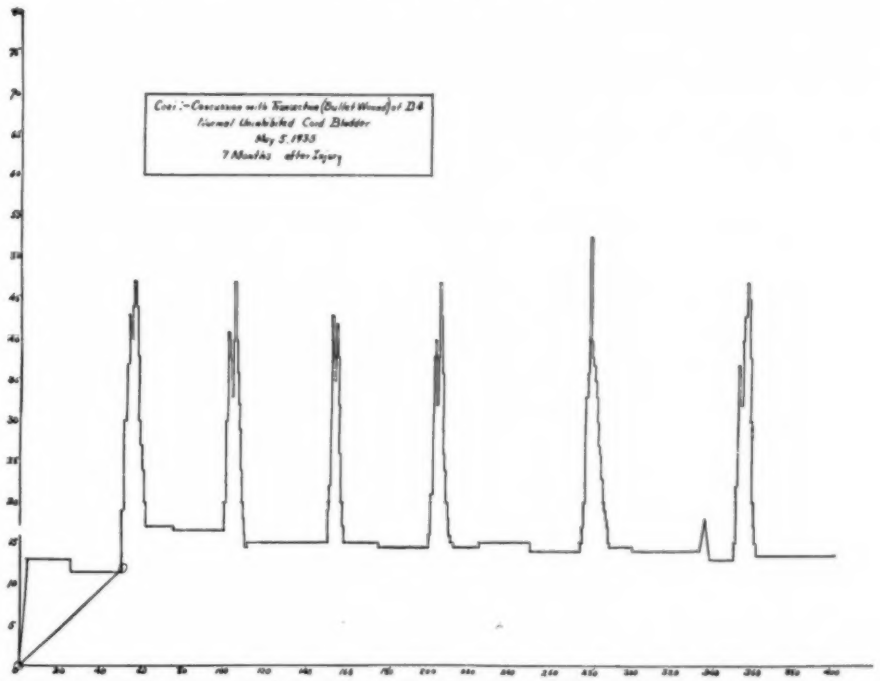

Fig. 7. Graph of an uninhibited reflex cord bladder. The abscissa indicates amount of fill and the ordinate the amount of intravesical pressure.

Treatment—they should be put on tidal drainage with the intravesical pressure forced to high levels. The siphon curve must be set 20 to 30 cm. above bladder level and even then there is prone to be leakage about the catheter until the bladder has been stretched a little. Until it can be done away with, any mild chronic urinary tract infection may cause such a bladder to regress or remain stationary in spite of treatment.

Treatment of The Normal "Cord Bladder." If progress is not interfered with by injudicious or insufficient treatment, the hypertonic "cord bladder" is succeeded by the normal "cord bladder." These are of two types depending on the nature of the original cord injury. Although, in the last analysis, both types may be considered objectively and subjectively normal by the ordinary tests it is possible by the comparison of cystometrograms of these bladders with those of known normal bladders to show differences in function between the two. I have differentiated them therefore as normal *cord* bladders in preference to speaking of them as normal bladders.

The Uninhibited Normal "Cord Bladder." The simplest of the normal "cord bladders" is the uninhibited. (Fig. 7.) It is present in all forms of cord injuries except the destructive lesions of the sacral segments and cauda equina. It is the normal end-result, as far as vesical function goes, in all cases of complete or nearly complete transection of the spinal cord above the level of the sacral segments. It probably represents what has been loosely spoken of in the past as the "automatic bladder" and is actually the expression of the normal fundamental uninhibited reflex activity of this organ. Subjectively and objectively, except by cystometry, it appears to be a normal bladder that empties itself completely at more or less regular time intervals. The initial tonus is three times that of the normal bladder. Instead of rising the sustained tonus falls to slightly below the starting level. Emptying contractions are constantly present and there is an absolute residual of only 6 per cent of the

fill. The storage capacity is below 200 cc. in 90 per cent of the cases. Since no inhibitory impulses reach the bladder, the emptying contractions are remarkably rhythmic and regular in occurrence. The external sphincteric activity is reflexly normal but not under voluntary control. Treatment is based on the use of a retention catheter. This is opened by the patient at intervals during the day and is attached to a tidal drainage apparatus at night. The length of the interval during which the catheter is shut off and the bladder allowed to fill from the kidneys is determined by experiment and varies with each patient. It will be influenced by the fluid intake and must be so arranged as to permit him to retain his bladder contents without leakage for as long a time as possible. In transection cases this is the best end-result that can be hoped for. (Fig. 8.) As a result the patient must be prepared to continue on this régime for the rest of his life.

COMPRESSION AND TRANSECTION OF LUMBAR CORD VERIFIED BY LAMINECTOMY
Case # Strand. Injured May 8, 1936—G. U. Tract Sterile—Kidneys Normal

Record of Cystometrograms

Date	Initial Tonus	Total Fill, Cc.	Sustained Tonus, Cm.	Capacity, Cc.	Emptying Contracts		Per Cent Residual	Reflexes	Type of Bladder
					Yes	No			
1936			Rise of						
May 8	13	400	1	400	..	+	0	?	Atonic
May 9	3.5	400	3.5	410	..	+	25	?	Atonic
May 10	6.5	400	20	450	..	+	37.5	?	Autonomous
May 15	10	400	37	425	..	+	25	?	Autonomous
May 24									
36° Post Op	8	400	25	400	..	+	35	+	Hypertonic
May 27	12	300	20	275	+	..	0	?	Hypertonic
June 19	12	200	18	250	..	+	0	?	Hypertonic
June 28	5	200	15	50	+	..	0	?	Uninhibited
July 9	6	475	13	130	+	..	?	?	Uninhibited
July 27	7	400	8	275	+	..	0	+	Uninhibited
Aug. 23	6	400	1	130	+	..	0	..	Uninhibited
Sept. 5	8	400	3	60	+	..	0	+	Uninhibited
Oct. 27	10	400	5	125	+	..	0	+	Uninhibited
Nov. 26	6	400	2	130	+	..	0	+	Uninhibited
Dec. 5	10	400	1	100	+	..	0	+	Uninhibited
Dec. 20	10	400	5	160	+	..	0	+	Uninhibited
1937									
Jan. 3	2.5	400	3	35	+	..	0	..	Uninhibited
Mar. 10	11	400	1	60	+	..	0	+	Uninhibited
Mar. 18	10	400	1	40	+	..	0	+	Uninhibited
Apr. 11	10.5	400	3.5	80	+	..	0	+	Uninhibited
Apr. 30	5	300	2	100	+	..	0	+	Uninhibited
Dehydrated June 28 to July 6, 1937—High temperature June 29 to July 8, 1937									
July 1	16	400	17	160	+	..	0	+	Hypertonic
July 17	10	400	1	85	+	..	?	+	Uninhibited
July 22	10	425	1	230	+	..	29	+	Uninhibited

Fig. 8.

The Normal "Cord Bladder" (Fig. 9). In all other types of cord injury this uninhibited cord bladder goes on to a stage that

differs from normal only cystometrically. The ability to inhibit emptying contractions is gradually regained and subjectively

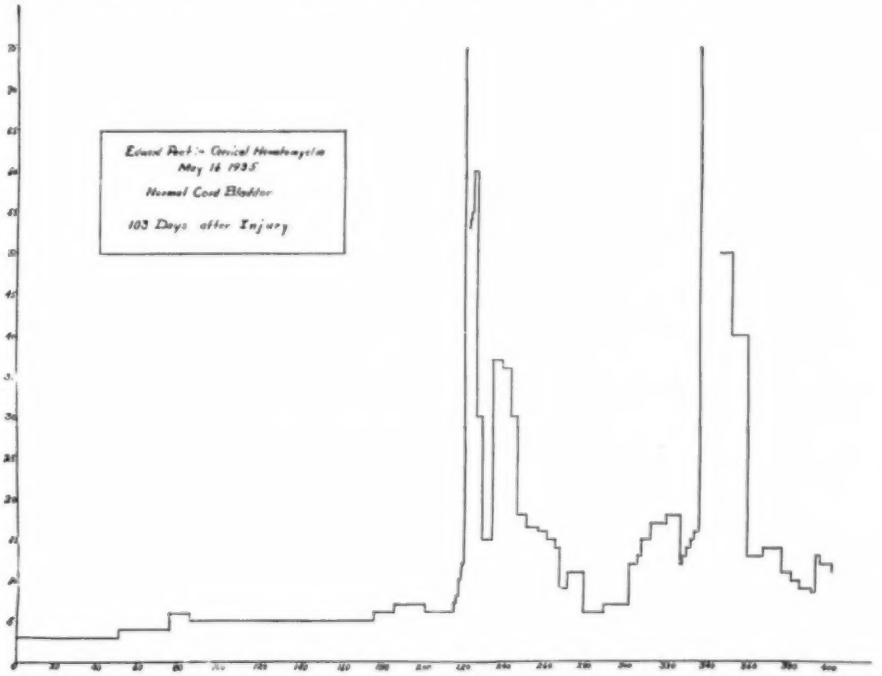

Fig. 9. Graph of a normal cord bladder. The abscissa indicates amount of fill and the ordinate amount of intravesical pressure. (Figures 1, 2, 3, 4, 5, 6, 7, 9 were published in *American Journal of Urology*, December, 1936.)

control of micturition is again complete. This requires a period of re-education, however, and treatment must be directed with that end in view. As a first step the bladder is drained at regular increasingly prolonged intervals. In this way the storage capacity will be increased and normal inhibitory impulses will be stimulated. In addition, whenever emptying is permitted, the catheter is only opened part way and the patient is made to actively expel his urine against a positive pressure. This serves as a further aid in helping him regain normal control of micturition. If possible these procedures are carried out with the patient in the upright position. Tidal drainage is used at first only at night and then dispensed with entirely. As soon as the patient can go three hours between emptying periods without leakage and provided he can of his own action completely empty his bladder against positive pressure, the catheter is removed. A further interval of training along the above lines follows with the idea that full nocturnal control and adequate day control shall be considered normal. (Fig. 10.)

Kidney function measured by intravenous pyelogram, phenolsulphonephthalein test, a retrograde pyelogram following cystoscopy, and repeated chemical and cystological examinations of the urine has proved to be normal in all such cases. Cystometrically, however, there still appears a variation from normal. The initial tonus is slightly higher than normal. The sustained tonus rises only 1 cm. as compared to a normal 7½ cm. in 400 cc. of fill. Emptying contractions may or may not be present in the normal bladder with this fill but are always present when 400 cc. is put into the normal *cord* bladder. Also in the latter residual urine is present to the extent of 16 per cent of the fill as opposed to a complete absence in the normal. The storage capacity is definitely greater in the normal bladder.

RESULTS

I have treated ninety spinal cord injuries during the seven years up to July 1, 1937.

These have been divided as follows: fifty-four cervical; twenty-one thoracic; and fifteen lumbo-sacral or cauda equinal. One hundred and ninety-eight cystometrograms have been made on this group. The constancy of the findings and the invariable response to treatment based on these findings, have been extraordinary. Tidal drainage of the urinary bladder in patients who have sustained a spinal cord injury has proved itself indispensable in my clinic and is used from the earliest possible moment. It will not work miracles. For example, it will not function when plugged with the débris of a badly infected bladder. Under such circumstances manual irrigation of the bladder has to be resorted to. It is not automatic. If it is set to care for an autonomous or atonic bladder, it will not function for a hypertonic type. It can not be used to its greatest advantage unless cystometrograms are made and used in conjunction with it. It has to be set up according to the specifications and it must be kept sterile.

LUMBO-SACRAL HEMATOMYELIA

Case # 2407. July, 1937. Ambulatory with Braces. Injured July 18, 1936—G. U. Tract Sterile and Normal—July 1937

Record of Cystometrograms

Date	Initial Tonus	Total Fill, Cc.	Sustained Tonus, Cm.	Capacity, Cc.	Emptying Contracts		Per Cent Residual	Reflexes	Type of Bladder
					Yes	No			
1936			Rise of						
July 20	4	400	6	520	..	+	100	0	Atonic
July 23	5	400	17	475	..	+	15	?	Atonic
July 26	9	400	13	700	..	+	35	+	Autonomous
July 31	16	400	29	400	..	+	0	+	Autonomous
Aug. 8	7	400	5	480	..	+	0	+	Autonomous
Aug. 29	6	375	10	110	+	..	?	?	Hypertonic
Sept. 6	5	400	5	95	+	..	8	+	Uninhibited
Nov. 19	6	400	11	325	+	..	0	+	Normal
1937									
June 15	Bladder is now and has continued to be normal								

COMPRESSION OF SPINAL CORD AT LEVEL OF 5TH CERVICAL VERTEBRA

Case # 2442. July, 1937. Leading Normal Life. Injured Sept. 18, 1936—G. U. Tract Sterile and Normal—July 1937

1936			Rise of						
Sept. 23	8	20	4	200	..	+	0	?	Autonomous
Oct. 5	5	400	4	190	+	..	?	?	Uninhibited
Oct. 27	7	400	−5	65	+	..	0	+	Uninhibited
Nov. 25	7	400	1.5	125	+	..	0	+	Uninhibited
1937									
Feb. 26	4	400	5	400	..	+	0	+	Normal
June 15	Bladder is now and has continued to be normal								

Fig. 10.

GENITO-URINARY TRACT INFECTION

Type of Treatment	Totals	Incidental to Treatment	From Technical Errors	Present before Being Seen	Final Per Cent of G. U. Tract Infection
Without tidal drainage	36	26	..	..	72.2
No urine examination.	19				
With tidal drainage...	35	5	2	1	14.2

Fig. 11.

Prognosis. Cystometry as described has proved of value as a prognostic agent. With the above experience as a background it can no longer be doubted that with an anatomical transection of the spinal cord at any level above the sacral segments and a complete absence of infection, the best that can be hoped for in bladder function is uninhibited reflex emptying (Fig. 8). This does not, however, mean invalidism for the patient. With tidal drainage at night and proper attention to their bladder at intervals during the day, such patients can be as active as their associated motor paralyses permit and should not suffer any diminution of their life expectancy. On the other hand, any other type of cord injury with the single exception of destructive sacral or cauda equinal lesions should, if properly treated, reach an end point with a functionally normal uninfected bladder. (Fig. 10.) Less than that is a reflection on the therapeutic ability of the surgeon who first saw the case and neglected to set up a tidal drainage apparatus and make cystometrograms at the earliest possible moment. The burden of explaining his failure to do so and the resultant poor end result lies squarely on his shoulders.

Results (Fig. 11). Without tidal drainage and regardless of the type of urinary tract therapy used—whether constant or intermittent catheter drainage, suprapubic cystotomy, or no drainage at all—there will be evidence of genito-urinary tract infection in over 72 per cent of patients with spinal cord injuries. This is based on a series of thirty-six cases of whom twenty-six were infected. On the other hand, with tidal drainage therapy as suited to cystometric variations of the individual bladders, there were only 5 infections of the genito-urinary tract present at the death or discharge of 35 similar patients. This is a comparable morbidity of 14.2 per cent.

CONCLUSIONS

For purposes of diagnosis, prognosis and treatment, "cord bladders" resulting from all types of spinal cord injuries should be divided into four distinct groups.

These may be measured cystometrically against normal bladder activity in terms of initial and sustained tonus, presence and periodicity of emptying contractions, the absolute amount of residual urine expressed in terms of percentage of fill, the storage capacity of the bladder and the reflex and voluntary sphincteric activity.

With these criteria, "cord bladders" are atonic, autonomous, hypertonic and normal.

The only permissible end-result of any "cord bladder" that results from spinal cord injury, is either an uninhibited "cord bladder" in cases of spinal cord transection above the sacral segments, an autonomous "cord bladder" in cases of destructive lesions of the sacral segments or cauda equina; or a normal "cord bladder" in all other spinal cord injuries.

All types of "cord bladder" are amenable to treatment by tidal drainage providing the apparatus is adjusted to suit the type of bladder being treated.

Except for complications due to misuse of the apparatus, tidal drainage as a method of treatment of "cord bladders" of any type has no contraindications.

Indwelling urethral rectal tubes used as catheters, or mushroom catheters, may be employed indefinitely in conjunction with tidal drainage in either male or female urethrae without producing cystitis or urethritis. They must be removed, cleaned, and replaced once a week and care must be taken to avoid the use of too large sizes.

Repeated cystometric examinations are essential in the treatment of all types of cord bladders and particularly if they are treated by tidal drainage.

The incidence of all types of urinary tract sepsis in spinal cord injuries has been reduced from 72 per cent in thirty-six cases to 14.2 per cent in thirty-five cases through the prompt, intelligent and routine use of tidal drainage in the care of the bladder.

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Congenital urethrorectal fistula results from failure of the urogenital fold completely to separate the rectum and posterior urethral segment of the bladder. This condition occurs about once in 7500 individuals and is twice as frequent in males as in females.

From—"Pediatric Urology" by Meredith F. Campbell, M.D.

INFILTRATING CANCER OF THE BLADDER INVOLVING THE TRIGONE—TREATMENT

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THE Thirty-eighth Aphorism of Hippocrates states: "It is better not to apply any treatment in cases of occult cancer: for, if treated, the patients die quickly; but if not treated, they hold out for a long time." Hippocrates must have been confronted with many cases of infiltrating cancer of the trigone to become so dispirited.

A review of the facts relating to 176 infiltrating cancers of the trigone, all included in the published reports of the Carcinoma Registry Committee of the American Urological Association, is of interest.

Of these 176 patients, all of whom were operated upon more than five years ago, only 19, or 11 per cent, survived three years; and but 13, or 7 per cent, were alive and without evidence of disease at the end of five years.

One hundred and fifty of the 176 patients were subjected to some form of surgical treatment in an attempt to cure their disease, with a post-operative mortality of 36, or 20.46 per cent.

From the record it might be surmised that these were cases in which the disease had already existed for a long time and in which the situation was nearly hopeless to start with. On the contrary, 88 of the 176 patients were observed or operated upon within six months of their first symptom, which in nearly every case was hematuria. Twenty-two of the patients were seen within one month of their first hematuria. All but fifty-two of the patients came under observation within one year.

Investigation of the detailed findings in these cases reveals some of the reasons why the results were no better, and points the way to improvement.

PATHOLOGY

The tumors with which we are concerned were infiltrating carcinomas involving part or all of the trigone. In each case the presence of the tumor resulted in obstruction, either partial or complete, to the urethra, one or both ureters, or all of these structures.

The tumors were highly malignant. Fifty-seven specimens were graded II, eighty-seven graded III, and thirty-two graded IV.

In many instances the tumor infiltrated the prostate or vesicovaginal septum, and in five cases spontaneous fistulae resulted.

These tumors metastasized early but the the metastatic manifestations of the disease were not often recognized in this series. A clinical diagnosis of metastatic carcinoma was made in but 12 of the 176 cases. Yet in 23 autopsies of 150 deaths metastases were found in 11, or nearly half. Fifteen of these autopsies were obtained after post-operative death and among these fifteen, metastases were found in five, but the metastatic disease had been recognized prior to operation in only two.

Spooner, in his review of the metastases found in 163 autopsied cases of carcinoma of the bladder, emphasized the above point as follows: "If, however, a considerable number of the patients who die after a short illness reveal metastasis at post-mortem examination, the incidence of metastasis should be important as a fairly reliable index of the metastatic lesions to be expected in similar groups of cases

in which the condition is considered operable."

In Spooner's series, as in the cases at present under examination, the primary disease was recognized relatively early. Thirty-eight and nine-tenths per cent of the Mayo Clinic patients had symptoms less than one year. Metastasis occurred in 49 of the 163 cases reported by Spooner, or 29 per cent. He remarks that only four of these forty-nine patients presented sufficient clinical symptoms to enable positive clinical diagnosis of metastasis to be made.

As in Spooner's series, the tumors here reported metastasized most often to the regional or abdominal lymph nodes, the liver, lungs, and more rarely to the bones. The higher incidence of metastasis in the present series as compared with the Mayo Clinic series is due to the fact that Spooner included all epithelial tumors of the bladder whereas this series deals only with the highly malignant tumors of the trigone. It is apparent that metastasis may be expected in this group of cases in approximately 50 per cent within the first year.

Pain not related to the act of urination, marked loss of weight, and vague gastric distress, are symptoms which were commonly associated in this series with the metastases discovered later. The presence of these symptoms should suggest a very thorough search both by physical and radiographic examination for the presence or absence of metastases.

INFECTION AND OBSTRUCTION

It is apparent that one of the chief factors contributing to the high postoperative mortality in infiltrating carcinoma of the trigone and to the poor end-results is infection.

The urine was examined microscopically in 143 of the 176 cases. Pus in sufficient quantity to be notable was found in 127. That this is a significant indication of serious upper urinary tract infection is evidenced by the examination of the reported causes of death in 102 of the 150 patients who succumbed to the disease or its complications.

Recurrence or metastatic disease led the causes of death with fifty cases so reported. Infection was responsible for twenty-eight deaths due to pyonephrosis, and seventeen deaths due to phlebitis, pelvic cellulitis, septicemia, or thrombosis and embolism. Renal failure due to the combination of obstruction and infection was the cause of death in sixteen cases. In some instances more than one of these causes was recorded as a sufficient cause of death.

Pyrexia, leucocytosis, pelvic or femoral phlebitis were commonly encountered as clinical manifestations of the severity of infection in the above cases.

The effect of the obstructing tumor on the upper urinary tract was evidenced by the fact that 51 of 109 patients were reported to have an increase in blood urea nitrogen above normal. It seems probable from the high incidence of pyonephrosis and obstructions of varying degree that palliative drainage of the upper urinary tract was indicated more often that it was performed.

The effect of the obstructing tumor or its infiltration of the bladder neck or prostate was responsible for many secondary operations. Among these, permanent suprapubic drainage or reopening of the sinus already present leads the list. In addition, six secondary prostatectomies were undertaken for obstruction, and seven operations were undertaken for the relief of obstruction to one or both kidneys. There were five nephrostomies and two nephrectomies.

TREATMENT

Whatever opinion one may hold as to the best method of treating carcinoma of the bladder, it is apparent from the above facts that judgment must be tempered with mercy. The patient and not the tumor should be given first consideration. The treatment of infiltrating carcinoma of the trigone in most instances will assume a palliative character, if the patient's best interests are to be served.

Accurate study of the location, size, and direct extensions of the primary tumor should center one's attention on the relief of the obstructing symptoms thereby produced. Thorough examination for the presence of distant metastases will result in the discovery of these lesions in a much higher percentage of cases than is usually supposed and lead to the conclusion that palliative therapy only is indicated.

Infection is present in varying degree together with renal insufficiency in an extremely high percentage of these cases. Before radical surgery or the radical application of physical measures are undertaken, the matter of infection and obstruction must be controlled by proper surgical drainage of the bladder, upper urinary tract, or in some instances, both.

When the patient is apparently free of metastatic disease, serious infection, or impaired renal function, or when the latter factors have been improved sufficiently by palliative therapy, radical treatment of the tumor may be considered. A biopsy should be taken to establish the character of the disease and the pathologist consulted as to the relative radio-sensitivity of the tumor. Many of the infiltrating tumors of the trigone are highly anaplastic and relatively radio-sensitive. The majority, however, are often squamous in character and relatively radio-resistant. Some surgeons will prefer complete cystectomy. Quinby has summarized the indications as follows: "The standards which I have set up for myself in regard to the suitability of a patient for a total cystectomy have been, (1) an involvement of the floor of the bladder so wide that if that malignancy were to be locally treated by any method, such treatment would involve the outlet of the bladder to such an extent that there would result loss of vesical function and incontinence; (2) I have insisted that there be no demonstrable metastases outside the bladder, and I have gone so far in each case, before subjecting the patient to a total cystectomy, as to investigate the retroperitoneal drainage area from the bladder, as a preliminary step. I have been much discouraged in more instances than I cared to believe possible to find involvement of the pre-aortic lymph nodes, or of the lymphatic channels leading up from the pelvis to that region. Of course, the patient is further studied by ordinary *x*-ray methods or whatever other method we have at our command to demonstrate secondary deposits. But in those instances in which one opens the peritoneum and investigates the retroperitoneal regions, it is surprising to see how often one will find them already the site of secondary deposits."

Others will prefer cystotomy and radon implantation and this method will meet with a measure of success in some cases, particularly when the tumor is of high grade and relatively anaplastic. When the tumor is small, it may be controlled cystoscopically by fulguration and radon implantation. When the tumor is large and cystectomy and radon implantation appear to be contraindicated, high voltage *x*-ray by the divided dose technique may secure a satisfactory palliative result. The good results in this series were obtained by all these methods. There is apparently no single best method for treating suitable cases of infiltrating carcinoma of the trigone. The selection of treatment must rest upon the peculiarities of the individual case and upon the experience and preference of the surgeon.

SUMMARY

Early infiltrating carcinoma of the trigone is a highly malignant disease. Metastases may be expected in 50 per cent of the cases within one year.

The obstructing tumor is attended by infection and renal insufficiency of sufficient degree to result in death in the majority of cases.

These cases should be regarded as palliative problems until they are definitely proved otherwise by the absence of detectable metastasis or the symptoms thereof, by the control of infection, and by evidence of a sufficient degree of renal function to

withstand any procedure proposed in the way of treatment.

In rare suitable cases a five-year cure may be obtained by a variety of methods, the selection of which must depend upon the individual case and the preferences of the surgeon.

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Syphilis of the ureter probably occurs more frequently than supposed, and is probably the cause of some strictures of the ureter.

. . . . . .

The symptoms of chief importance in polycystic kidney are tumor, pain and signs of renal insufficiency.

From—"Modern Urology" Edited by Hugh Cabot, M.D., C.M.G., F.A.C.S.

URETERO-INTESTINAL IMPLANTATION: INDICATIONS AND METHODS

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THE problem of uretero-intestinal implantation has not changed greatly in the last decade, though the former fear of peritonitis is no longer present. All surgeons today realize that peritonitis results from leakage after implantation and seldom is caused by contamination at the time the bowel is opened for implantation. The real dangers are renal, either from ureteral obstruction at the site of implantation or from ascending infection after operation. The risk of the procedure, therefore, is the possibility of early death from surgery or later from renal sepsis or insufficiency. In spite of these dangers, however, there has been a definite increase in interest throughout the world in uretero-intestinal implantation, particularly in connection with the treatment of cancer. Used in this connection, the risk is naturally increased. A recent analysis* of the literature on uretero-intestinal implantation, from 1851—when the procedure was first attempted by Simon—to 1936, showed an operative mortality of 30 per cent in 740 patients. Four hundred and ninety of the 740 patients had benign conditions (exstrophy, etc.); 203 had cancer; the diagnosis was not stated in 47. The operative mortality in the benign group was 20 per cent as compared with 50 per cent in the patients with cancer. Perhaps an analysis of cases in the last decade would show a definite improvement. At any rate there is a general feeling among surgeons today that the risk is not nearly so great as these statistics indicate. This accounts for the interest in the problem.

With modern methods and better understanding the risk does not appear to be prohibitive. This risk has to be balanced against the alternative course of treatment and the miserable condition of many patients unless uretero-intestinal implantation is performed. Except for this operation, the only methods of deviation of the urine are nephrostomy and transplantation of the ureters to the skin. The first is often of extreme value as a temporary procedure, but the latter is regarded by most surgeons as adding little to the comfort of the patient. When successful, uretero-intestinal implantation is most satisfactory and gives continence and complete comfort. It seems to be fully justified under certain carefully selected conditions.

The indications for uretero-intestinal implantation fall into two groups; namely, benign and malignant conditions. Among the benign conditions in which uretero-intestinal implantation is indicated are the anomalies of development with incontinence which cannot be relieved otherwise. Of these, exstrophy is commonest and the use of implantation of the ureter into the bowel in this condition has been most satisfactory. With the submucosal method of Coffey or some modification of it, even when results of all surgeons for all time are grouped together, the surgical mortality has been 15 per cent and, during the last 10 years, it must have been considerably lower. Even with this mortality the operation is recognized as a blessing to all patients with this condition which,

* HINMAN, FRANK and WEYRAUCH, HENRY M., JR. A critical study of the different principles of surgery which have been used in uretero-intestinal implantation. *Trans. Amer. Assoc. of Genito-Urinary Surgeons* (1936) pages 15–156. See also Internat. Abstract of Surgery. *Surg. Gynec. & Obst.*, 64: 313–363, (April) 1937.

without it, will render a much shortened life miserable. The question arises as to how early patients with exstrophy may be operated on. Theoretically, other things being equal, the sooner after birth the operation is performed, the less is the risk of urinary infection. To test this idea, the writer operated on two patients under one year of age, the youngest being four months old. At this time the ureters are of a favorable size but the wall of the intestine is thin and underdeveloped, rendering implantation more difficult and insecure. Infants of this age do not seem to stand surgery so well as when older. It would seem advisable never to attempt implantation until after the age of one year at least.

Some conditions of acquired incontinence which cannot be relieved otherwise are suitable for uretero-intestinal implantation. Occasionally a vesicovaginal fistula, for which repeated attempts at closure have been unsuccessful, falls in this group; as do also other traumatic lesions of the urethra and neck of the bladder, which cannot be repaired. Another acquired condition occasionally requiring consideration is prolonged vesical dysfunction and pain occurring with incurable types of infection, contraction, etc.

The malignant conditions include all those in which diversion of the urine would permit their radical removal. Cancer of the bladder is the commonest. Two definite types of cancer are now recognized—papillary and sessile tumors. The papillary tumors consist of the benign and malignant papillomata and the papillary carcinomata; distinguished mainly by the fact that in the latter group the base of the tumor and adjacent wall of the bladder are invaded and infiltrated by cancer. Benign and malignant papillomata can be cured by fulguration and diathermy and some papillary carcinomata apparently disappear under intensive diathermy. Radium has been extolled in these two conditions but, under either form of treatment, with persistent recurrence, a more radical means of treatment often is indicated. Few of the flat sessile tumors are radiocurable either with radium or deep *x*-ray so that, given a malignant tumor of the bladder which obviously cannot be cured by fulguration or diathermy, total cystectomy should be considered. The life of a patient with cancer of the bladder is often prolonged by various types of irradiation. The miserable existence of many of these patients, however, hardly justifies this prolongation. It is true that many of these tumors are situated on the dome or lateral walls, giving the opportunity of resection with a wide margin of healthy bladder wall. Resections of tumors, the majority of which are friable and break up easily on manipulation, do not give a high percentage of cure because of the frequency of implantation of cells at the time of resection. The age and the physical condition of the patient are of importance in making the decision to implant ureters and to perform cystectomy. The earlier the diagnosis, the higher will be the percentage of cures. Too long delay of course has allowed the tumor to spread beyond the bladder to form lymphatic and visceral metastases so that any method of procedure then would not cure the patient. Many of the poor results with total cystectomy are due to this fact and not to the primary risk of uretero-intestinal implantation. If the advice for cystectomy comes late, it frequently will be found at the time of operation that the pelvis is frozen with cancer or that the malignancy has infiltrated so as to make dissection difficult, prolong the operation, and cause extensive bleeding. Death results from the effects of cystectomy and not from uretero-intestinal implantation. Other malignant conditions which occasionally give indications for preliminary uretero-intestinal implantation are: cancers of the urethra, particularly in the female, cancers of the vagina with invasion of the bladder, and cancers of the prostate with invasion of the neck of the bladder, radical removal of which would seem impossible by Young's

perineal method. In the use of uretero-intestinal implantation in connection with cancer of any kind, careful selection of the patient who does not have metastases is of first importance. The more carefully this selection is made, the higher will be the percentage of cures.

The operation is not applicable in conditions in which there is any defect in the control of the rectal sphincter. Urinary incontinence with spina bifida, for instance, is common, but most of these patients also have fecal incontinence. When the rectal mechanism is competent, the control of urine after ureteral implantation is entirely satisfactory. Patients will go from four to eight hours and usually will empty the urinary and fecal contents of the bowel separately and are themselves able to distinguish between these two functions.

The indications for uretero-intestinal implantation, therefore, are usually definite and, when the operation is successfully performed, the results are entirely satisfactory. In connection with cancer, the problem is distinctly two-fold, the first part related to the success of implantation and the second to the degree of success in the removal of cancer.

The Technique of Uretero-intestinal Implantation: More than sixty methods of implanting the ureter into the intact intestinal tract have been described in the literature by more than fifty-five surgeons. None of these methods is particularly outstanding when judged by the results, and the differences between many of them are so slight and the methods so numerous that comparison of results is difficult. When these operations are grouped according to the chief principle of surgery upon which they are based, certain differences become manifest. The grouping according to principle is sometimes difficult because one operation may combine several principles. The surgical principle used with the idea of preventing some complication which might arise from the intestinal tract, as, for instance, peritonitis and intestinal obstruction, should be distinguished from the principles proposed primarily to prevent uretero-renal complications. When the principles developed particularly for control of uretero-renal complications are placed foremost, the sixty-odd methods can be grouped under eleven headings. These have been reviewed, in the article referred to above, as the eleven surgical principles which, when arranged chronologically, are as follows:

1. The formation of a fistulous tract (1851)
2. The direct anastomosis of ureter and bowel (1878)
3. The muscularizing principle
   (a) to prevent leakage (1886)
   (b) stripping action (1899)
4. The preservation of the ureterovesical orifice (1892)
5. The temporary diversion of urine until healing has occurred (1892)
6. The use of a flap to act as a valve (1895)
7. The use of mechanical devices (1895)
8. Implantation into structures which open normally into the gastro-intestinal tract (1900)
9. The submucosal principle (valve action) (1910)
10. Temporary colostomy (1915)
11. The use of the intact ureter (1931.)

All of the sixty-odd methods can be grouped under these eleven headings. They have been discussed fully elsewhere and will be indicated here only in outline:

The First Surgical Principle. The Formation of a Fistulous Tract between the Ureter and the Bowel.

a. In cases of extrophy by a long suture connecting the lumen of the ureter to the lumen of the bowel.
   Simon (July, 1851),
   Lloyd (October, 1851).
b. By a submucosal tunnel in the intestinal wall.
   (Kirwin, 1930, experimental.)
c. By the transfixion suture
   1. With submucosal implantation. Ninth surgical principle. (Coffey, No. 3, 1930.)

2. With the intact ureter. Eleventh surgical principle (Higgins, 1933).
3. With temporary drainage by ureterostomy. Fifth surgical principle. (Hinman, 1935.)

d. By perforation of apposing surfaces with the cautery, in conjunction with the use of the intact ureter. Eleventh surgical principle.
(Ferguson, 1931, experimental.)
(Poth, 1935, experimental.)

e. By the electric coagulation of apposing surfaces without perforation. Experimental.
(Wadhams and Carabba, 1935.)

f. By the transfixing hair pin method in conjunction with the intact ureter (eleventh principle).
(Brenizer, 1935.)

The Second Surgical Principle. The Direct Anastomosis of the Ureter and Bowel.

a. The direct anastomosis of mucosa to mucosa.
1. Using the end of the ureter (end to side).
(Smith, 1878; Chaput, 1892.)
2. Suturing a slit in the side of the ureter to a slit in the side of the bowel (side to side).
(Peterson, 1900.) Experimental.

b. Axial implantation of the ureter without the suture of mucosa to mucosa.

The Third Surgical Principle. The Muscularizing Principle.

a. Overlapping of the intestinal wall to form a muscular canal around the ureter (as around Witzel's gastrostomy tube, 1891).
(Bardenheuer, experimental, 1886, clinical, 1887; Depage and Mayer, 1904; Tichoff, 1905; Stiles, 1907.)

b. A muscular canal around the ureter beneath the serosa (stripping action).
(Martin, 1899.)

c. With preservation of the ureteral orifice. The fourth principle.
(Jefferson, 1908.)

The Fourth Surgical Principle. The Preservation of the Ureterovesical Orifice.

a. By transplantation of the trigone with both orifices intact.
(Maydl, 1892; Moynihan, 1905.)

b. By transplantation of each orifice separately in the form of a rosette.
(Bergenhem, 1894; Jaja, 1901.)

The Fifth Surgical Principle. Temporary Diversion and Drainage of Urine.

a. By ureteral catheters transrectally.
1. With axial implantation. The second principle.
(Giordano, 1892, experimental.)
2. With preservation of ureteral orifices. The fourth principle.
(Peters, 1899.)
3. With submucosal principle. The ninth principle. (Coffey, 1925.)
Modified by Furniss, 1930; Nitch, 1932; Green-Armytage, 1932.
4. With intact ureter. The eleventh principle. (Ferguson, 1931.)

b. By preliminary nephrostomy. (Heitz-Boyer and Hovelacque, 1912; Hinman, 1926.)

c. By extraperitoneal ureterostomy with a transfixion suture. The first principle.
(Hinman, 1935.)

The Sixth Surgical Principle. The Use of a Flap to Act as a Valve.

a. Of the entire intestinal wall. (Vignoni, 1895, experimental.)

b. Of submucosa and mucosa. (Fowler, 1896.)

c. Of the trigone. The fourth principle. (Pisani, 1896, experimental.)

The Seventh Surgical Principle. The Use of Mechanical Devices.

a. The button of Boari. (1895.)

b. The copper tubes of Chalot. (1896.)

c. The bobbin of Evans. (1899.)

d. The "dress-snap" of Zollinger (1934) experimental.

The Eighth Surgical Principle. Implantation into Structures which open Normally into the Gastro-intestinal Tract.

a. Appendix. (Roux, 1900; Eaton, 1910.)

b. Pancreatic duct. (Baird, Scott and Spencer, 1917, experimental.)

c. Gall-bladder. (Dardel, 1922, experimental; Kehl, 1923, experimental.)

The Ninth Surgical Principle. The Submucosal Principle (Valve Action).

a. The triangular exposure of the submucosa. (Krynski, 1896, experimental.)

b. Coffey's technique No. 1 (experimental, 1910; clinical, 1913).

(After method of Coffey [1909] of submucosal transplantation of the common bile duct into the intestine.)

c. Mayo's modification (catgut urine guide. 1912.) (Coffey-Mayo operation.)

d. Cabot's extraperitoneal modification of Coffey's technique No. 1. (1921.)

e. Coffey's technique No. 2 (1925) with catheter drainage. The fifth surgical principle.

Mayo's catgut guide.

Ward's catheter splint. (1937.)

f. Furniss' modification (1928) preserving peritoneal attachment.

g. The modification by the use of approach tunnels.

Mayo, 1930.

Papin, 1930.

Walker-Taylor, 1930. Open tunnel (first plan), closed tunnel (second plan); aseptic irreversible tunnel (third plan).

h. Coffey's technique No. 3 with transfixion suture. (1930.) The first surgical principle.

i. The simple aseptic method with a divisible carrier. (Hinman, 1935.)

j. Aseptic submucosal transplant by use of an electric snare. (Foley, 1936.)

k. Aseptic submucosal transplant by use of a barb. (Palmer, 1936.)

The Tenth Surgical Principle. Temporary Colostomy.

a. For the purpose of direct inspection and treatment of the site of implantation. (Barber, 1915.)

b. Preliminary to implantation for the purpose of sterilization of the bowel and after implantation for the temporary diversion of the feces. (Nesbit, unpublished; Higgins, 1931.)

The Eleventh Surgical Principle. The Use of the Intact Ureter; A Two-stage Operation.

First Stage: A loop of ureter is isolated and an intact section is imbedded down to the submucosa beneath the muscular layers of the bowel. (Urine continues to drain into the bladder as usual.)

Second Stage: The lumina of the ureter and bowel are connected.

a. By a fulguration tip inserted through the proximal end of the ureter divided just below the point of its egress from the submucosal channel. (Ferguson, 1931, experimental; Poth, 1935, experimental.)

b. By insertion of the proximal end of the divided ureter into the lumen of the bowel through an opening made at the point of egress of the ureter from the submucosal channel. (Ferguson, 1931, experimental; Winsbury-White, 1933; Nesbit, 1935.)

c. By a transfixion suture placed at the first stage. (Higgins, 1933.)

d. By hair pin wires looped over and through the ureter. (Brenizer, 1935.)

e. By insertion of the end of the ureter by the use of a barb. (Palmer, 1936, experimental.)

When one compares the results achieved by the various methods mentioned, it is found that three principles have been used most widely: the muscularizing principle (third) has been applied in operations on 136 patients, with a surgical mortality of 27.9 per cent; the preservation of the ureteral orifice (fourth) in 243 patients with 27.6 per cent mortality; and the submucosal principle (ninth) in 259 patients with a surgical mortality of 30.1 per cent. If these three groups are separated as to benign and malignant conditions, the surgical mortalities for the three principles respectively are as shown in Table 1.

A study of the literature leads to the feeling that the submucosal principle is the most vital to success in uretero-intestinal implantation. It is doubtful, however, whether it is, in any way, a surgical imitation of the ureterovesical valve. Its virtue

lies more in the fact that it is a simple and sound way to prevent leakage and furthermore it is the only natural route for the entrance of the ureter into the bowel. A study of the literature leaves one with the feeling also that the simpler methods are superior and this is supported by personal experiences with fifty-nine patients in whom the writer has implanted one or both ureters into the bowel. The preparation of the patients, the preparation of the bowel, the type of anesthesia and the aftercare are all extremely important factors to success by any method. The following table (Table II) shows an analysis of personal cases, twenty-four patients operated on for benign conditions and thirty-five for malignant. Of the patients with malignancy,

TABLE I

Submucosal				Muscularizing				Maydl		
Benign		Malignant		Benign		Malignant		Benign		Malignant
No. of Patients	Per Cent	No. of Patients	Per Cent	No. of Patients	Per Cent	No. of Patients	Per Cent	No. of Patients	Per Cent	
143	15.5	110	48.2	92	19.5	44	45.4	243	27.6	Not applicable

TABLE II

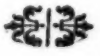
59 PERSONAL CASES OF URETERO-INTESTINAL IMPLANTATION

	No. of Cases	Carcinoma of the Bladder		Tuberculous Cystitis		Vesico-vaginal Fistula		Exstrophy of the Bladder		Hunner Ulcer	Summary	
		35		7		4		12		1	59 Cases	
		Dead	Living	Dead	Living	Dead	Living	Dead	Living	Dead	Dead	Living
Modified first method of Coffey	8	1	1	..	4†	..	..	..	2	..	1	7
Second technic of Coffey (catheter drainage)	15	4	1	..	..	2	1	2 1* 3	3	1	10	5
Third technic of Coffey with extraperitoneal ureterostomy	3	1*	1	..	1	..	..	..	..	..	1	2
Total	26	6	3	..	5	2	1	3	5	1	12	14
Simple seven suture method	33	15	11	..	1 1† 2	..	1	1	3	..	16	17

* After cystectomy.
† With nephrostomy.

twenty-one are dead and fourteen are living. All but four of these patients had carcinoma of the bladder. One had a urethrovaginal cancer and three, cancer of the prostate with extensive invasion of the neck of the bladder. Four of the deaths were definitely the result of carcinomatosis. Fourteen patients are living. An answer to a questionnaire has been received from only ten. An attempt is now being made to get definite replies from the others so that analysis of these surviving patients will be of value.

This personal experience with cancer teaches the value of early diagnosis and operation. The writer has a distinct feeling that in too many of these patients the condition was really inoperable, as evidenced by the great difficulty in removing the bladder and the frequency of death from generalized carcinomatosis afterwards. Nevertheless, as shown by the findings at autopsy, three fatalities were caused by error in technique, which allowed leakage at the site of implantation. It is also evident from a study of these few cases that, when uretero-intestinal implantation is done in order to permit radical surgery for cancer, most of the fatalities follow the surgery for removal of the cancer rather than the transplantation. One lasting impression is that the simpler methods are far superior to the complicated ones.



From an embryological stand-point, the testicle and the kidney are much alike, and there is ample proof that the latter may allow the passage of tubercle bacilli and other organisms without injury to itself.

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DISEASES OF THE URETHRA IN THE FEMALE

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ADDED attention to the frequency and significance of lesions of the urethra in the female has emphasized the importance of this short structure in its relation to urinary dysfunction. No consideration of urethral pathology in women can be complete without a proper correlation of affections of the cervix uteri, uterus, uterine adnexa, remote foci of infection and neurological lesions. In a study of 1,000 women with frequency of urination, Bugbee[1] stated that lesions of the urethra were partially or solely responsible in 690 instances. Stevens,[2] in analyzing 234 consecutive cases of urinary disturbances in women, described the urethra as wholly responsible for the symptoms in 56 and partially responsible in 173. Many other recent contributions on this subject evince an increasing recognition of the importance of urethral lesions in women.

Proper examination of the female urethra should include a careful inspection of the unwashed meatus and para-urethral ducts. Purulent discharge, if present, should be carefully examined by stained smear. It not infrequently happens that extra-urethral ducts are infected with gonococci, while the urethra itself is free of infection. The anterior third of the urethra may be inspected by eversion of the urethral lips or, if indicated, by means of a "skenoscope." This instrument allows a more thorough inspection of the para-urethral ducts and often secretion is seen and obtained at the orifices of these ducts when it could not be secured after manual stripping. When gonococci cannot be demonstrated, the urethral lumen should be calibrated with woven silk-elastic olive tipped bougies. Single strictures occur just inside the external meatus. For this reason, woven bougies may buckle and a similar metal instrument is sometimes to be preferred for calibration. Urethroscopic examination is made, in the absence of low caliber stricture, in the manner and with the instrument suited to the individual examiner.

Malformations: Absence of the urethra is rarely observed. When present it is usually associated with other anomalies, such as exstrophy of the bladder or patent urachus.

Double urethra is also a rare anomaly and may be complete or incomplete. Bifurcation of the urethra, in which a single urethral canal arises from the bladder and divides into two canals with separate openings on the vestibule, is more common than two distinct channels. Double urethra must be differentiated from peri-urethral fistula and ureteral ectopia.

Epispadius is a congenital deformity of the urethra in which there is a partial or complete absence of the superior wall. The symptoms are those of partial or complete urinary incontinence with dribbling of urine and irritation of the adjacent skin surfaces. Treatment is entirely directed at plastic repair of the defect.

Hypospadius, which is a pathological rarity, is a defective development of the external portion of the inferior urethral wall by which the external meatus appears as an oblique opening on the anterior vaginal wall. Only about forty cases are recorded. There are no symptoms of this anomaly if the sphincter is active and if the meatus is well forward on the anterior vaginal wall. If the hymen is intact, the urine may flow into the vagina and dribble from the vaginal orifice. Stricture at the meatus occurs frequently and requires dilatation with bougie or sound. Plastic

surgery is required to cure incontinence and reconstruct the urethral canal.

Injuries of the female urethra may be classified as being due to trauma incident to childbirth, external violence, catheterization and instrumentation, and surgical operations. The sequela of childbirth may be a weakened urethral wall with dilatation of the lumen or, in contrast, there may be a chronic infiltration with fibrosis and stricture formation. Such injuries to the urethral muscles may result in weakening their contractile power with subsequent, immediate or long delayed, partial incontinence of urine.

Prolapse of the urethra designates an extrusion of the mucous membrane through the external meatus. The condition may be partial or incomplete but usually the entire circumference of the urethral mucosa protrudes. Prolapse results from prolonged or repeated straining, such as occurs in tedious labors, difficulty in voiding or in defecation. Its occurrence is probably dependent upon the fact that in some women there is an abnormal redundancy of the mucosa which is not firmly attached to the underlying structures. Prolapse is most common in the extremes of life. The subjective symptoms are those of a tender, easily bleeding external meatus and a burning pain on urination. Caruncle, polypi, new growth and inflammatory swellings must be differentiated from prolapse. Treatment consists of excision of the redundant mucosa, stellate fulguration, or interlinear deep coagulation of four equidistant portions of the external protrusion.

Diverticulum, or urethrocele, is a pouch or sacculation formed by dilatation of a circumscribed portion of the inferior wall of the urethra. When the protrusion presents all layers of the urethral wall it is called a "true" diverticulum. When only the layers of the submucosa and mucosa are present in the sac, it is known as a "false" diverticulum.

These diverticula are considered as being either congenital or acquired. The condition occurs most commonly in women who have borne several children and in whom repeated traumatisms to the anterior vaginal wall have injured the urethral musculature. Inflammatory closure of the urethral gland ducts with resultant retention cysts which suppurate and perforate the urethral wall may give rise to false diverticula.

The symptoms are those of painful and frequent urination, pyuria, tenderness in the anterior vaginal wall and a purulent urethral discharge. Dribbling for a sufficient time to empty the sac may follow each voiding.

The protrusion may be seen as a tumefaction upon the anterior vaginal wall. If the orifice of the diverticulum is large, pressure upon the vaginal aspect gives a sense of a fluctuant cyst and its contents may be easily expressed into the urethra and flow out of the external meatus. If the urethral opening is small or obstructed by calcareous material, the tumor feels hard and firm and the contents cannot be completely expressed. Diagnosis is made by inserting a probe or small sound into the urethra and palpating the region vaginally. Urethroscopic examination may permit vision of the orifice and allow insertion of an opaque ureteral catheter or the injection of opaque solution for outline of the diverticulum on a roentgenogram.

Differential diagnosis includes cysts of the vaginal wall and vesicovaginal septum, calculus retained in the urethra and various degrees of cystocele. Shivers and Cooney[3] report the occurrence of a large calculus in a urethral diverticulum. They found only twenty-two such case reports in the literature.

The ideal method of treatment is the total excision of the entire sac through a vaginal incision. The urethral wall is then closed over a catheter or sound and the vaginal layers approximated below. Because of infection in the diverticular sac, healing after excision and suture may be difficult. For this reason Shivers and Cooney recommend diversion of the urine

through suprapubic cystostomy for a period of at least eighteen days.

Neoplasms of the female urethra may be classified as follows: *Benign*—caruncle, polypus and papilloma. *Malignant*—epithelioma, carcinoma, adenocarcinoma (rare) and sarcoma (very rare).

Of the benign lesions *caruncle* is the most commonly seen. The term "caruncle" includes the various types of mucous polypi which take origin at the meatus. They usually arise from a broad base or slender stalk and practically always take origin on the floor. Histologically, caruncles are either papillomatous or angiomatous. Clinically, a caruncle may be very tender and troublesome or the patient may not even be aware of its presence. Urination may be frequent and very painful. Caruncle must be properly treated or it will recur at the base. The most satisfactory method of treating these growths is complete dessication with a high frequency current. Excision, with cauterization of the base, is preferred when there is the slightest suspicion of carcinoma. Biopsy should always be done in this group.

Polypi and benign papillomata of the urethra are merely hypertrophied projections from the mucous surface. They are commonly found in all parts of the urethra but more frequently are seen along the margin of the internal sphincter. These excrescences are the result of long continued bacterial irritation of the urethra due to preceding urethritis or pyelocystitis. Evaluation of the importance of these lesions is difficult. Large villi are frequently seen in the absence of any symptoms and again a few small polypi seem associated with severe tenesmus and frequency. These areas are best visualized by an open ended, semi-direct or direct instrument. Here again treatment should be complete destruction by electrocoagulation visually applied. One should never be content to explain a questionable source of hematuria by the discovery of these polypi. Before placing the blame for symptoms or hematuria on these vascular excrescences, the bladder and upper urinary tract should be carefully studied.

Carcinoma of the urethra is not nearly the uncommon lesion one would presume from a survey of the literature. Counseller and Paterson,[4] in 1933, found 136 authentic cases of primary carcinoma of the female urethra and added 12 instances from the Mayo Clinic.

Carcinoma of the urethra should not be confused with carcinoma originating in the vulval or vaginal wall. Primary carcinoma of the female urethra most frequently develops in the mucosa of the urethra and is usually of a squamous cell type, of higher malignancy than is commonly found on other cutaneous surfaces. There are no characteristic symptoms of urethral carcinoma, except the appearance of the growth itself. Urethral bleeding and pain on urination prompt the patient to seek advice. Examination reveals a sessile papillary growth protruding from the meatus. This may be smooth and indurated or ulcerated and sloughing. Differential diagnosis includes chronic hyperplastic urethritis, caruncle, polypus and prolapse of the urethra. Three methods of treatment, alone or in association, are available for the treatment of tumors of the female urethra: surgical excision, deep electrocoagulation and irradiation by radium or Roentgen rays. Because of the lack of sufficient material warranting any one observer in drawing definite conclusions, conflicting views are held as to adequate treatment. The author has six patients with an apparent cure of from five to nine years after coagulation alone, one other eight years after coagulation and topical application of radium. The latter practically always brings about stricture and, since most of these growths are radioresistant, it would seem that Roentgen ray and radium will only add to the patient's suffering. Each woman who survives surgery, electrocoagulation or irradiation is a candidate for treatment of stricture of the urethra for the rest of her life.

Stricture of the female urethra may be congenital or acquired. Acquired strictures are the result of localized inflammatory processes or of traumata. Gonorrhea, urethritis of non-specific origin with para-urethritis, ulceration of syphilis or chancroid bring about the ultimate sclerosis. Traumatic strictures are found both at the external meatus and in the lumen of the canal. Cicatricial narrowings in these cases are the result of traumatism occurring during childbirth or surgical procedures. Fulguration, chemical cauterization or irradiation may produce stricture. Stricture of the female urethra seems to be responsible for a wide variety of symptoms: frequency of urination, small stream, pain, urgency, difficult micturition, sense of residuum after voiding, partial incontinence or dribbling may be the associated symptoms. As many patients with stricture have an associated urethritis or cystitis, the general symptoms are those of urinary tract infection. The diagnosis of urethral stricture is made by calibration of the urethral lumen. Normally the adult female urethra admits without "hang" a 24 F. bougie à boule. Gentle dilatation of the urethra by the passage of progressively larger sounds, or bougies, is the method of choice.

Inflammations of the female urethra are due to infections with the gonococcus or to pyogenic bacteria of a non-specific character.

Acute non-gonococcic urethritis is usually associated with repeated traumatism or irritation, such as occurs in the frequent use of catheter or with overzealous exploration or treatment; it may also be associated with indwelling catheter, calculi or other foreign bodies. Colon bacilli, staphylococci and streptococci are the common organisms found. Trichomonas vaginalis is frequently found in the female urethra and cervix. The exact significance of this parasite is far from clear. Often, when it is discovered, there are no associated symptoms. It has been repeatedly stated that trichomonas is an innocuous companion of the streptococcus in urethra and cervix, although some believe that it causes primary inflammation.

Acute gonococcic urethritis is an affection of the mucous membrane and para-urethral ducts. Acute symptoms are usually short lived, lasting from three days to three weeks in untreated cases. This discomfort is often so slight that the patient ignores the symptom unless accused or appraised of the fact that the gonococcus has been found. Treatment of acute urethritis is palliative or active. Palliative measures include rest, hot sitz-baths, alkalis and urinary sedatives. Active measures include urinary antiseptics, methenamine, mandelic acid and sulfanilamide, foreign protein injections, bouillon-filtrate injections, pyrexia or other types of heat induction. The main complication of gonococcal urethritis is infection of the paraurethral glands or "Skene's ducts," and it is this type of infection which predominates in so-called chronic urethritis. Local cauterization or coagulation of the para-urethral ducts should not be attempted until the acute urethritis has subsided. Sub-urethral abscess is a rare complication of acute or chronic urethritis.

The present tendency in the treatment of both acute and chronic urethritis is away from prolonged or repeated topical treatment and toward amelioration of local symptoms by chemotherapy or by increasing general rather than local immunity. Destruction of any persistent nidus of infection is then carried out by coagulation or desiccation of the affected area. Intelligent and diligently applied treatment is now curing urethritis, especially the gonococcal, with the same precision that localized infections are being eradicated in other parts of the body.

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ELUSIVE ULCER (HUNNER) OF THE BLADDER WITH AN EXPERIMENTAL STUDY OF THE ETIOLOGY*

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INTRODUCTION AND HISTORY OF TERMINOLOGY

THE great variation of treatment and, on the whole, the unsatisfactory clinical results, have prompted us to a further study of the etiology of the elusive bladder ulcer of Hunner.

Ulceration of the bladder may vary from the slightest inflammatory change in the mucosa to an ulcerative cystitis of the entire bladder wall. The more common forms of ulcerative cystitis are easily recognized and readily placed on a definite etiological basis. The ulcer of Hunner, however, has given some difficulty both in ascertaining the cause and in diagnosis.

A great diversity of terminology has arisen to designate the lesion. In 1914, it was described by Hunner[1] as a "rare form of bladder ulcer." He was the first to demonstrate the lesion in this country. It had been pointed out by Nitze[2] in Germany, in 1907, and named by him "cystitis parenchymatosa." The term "elusive ulcer" was offered by Cullen because of the difficulty sometimes experienced in diagnosing the lesion. "Paracystitis" was proposed by Geraghty,[3] and Keen[4] suggested the more comprehensive term "circumscribed panmural ulcerative cystitis." On the basis of the pathology, the terms "panmural fibrosis"[5] and "submucous ulcer"[6,2,10] have been interchangeably used by the Mayo Clinic group.

One of us (G. B.) has suggested the term "bladder fissure" because in the first place it is not a true ulcer, and in the second place because of the striking similarity to rectal fissure. The similarity is apparent in the symptomatology; both are extremely painful and bleed on dilatation. Therapeutically both are relieved to some extent by silver nitrate, phenol, fulguration, dilatation and in the last analysis, by resection. Pathologically, both produce a fibrosis with a contracture of either bladder or rectum, respectively. Microscopically both show infiltration of plasma cells, round cells, engorged capillaries and proliferation of connective tissue.

The lesion occurs most frequently in the middle decade of life. Hunt[7] reports an age range of 28 to 56 in their series at the Mayo Clinic. The average age of onset of symptoms was 37; in Crenshaw's cases it was 47.[5] The duration of symptoms may be from a few weeks to many years, indicating that the lesion is often resistant to any type of treatment.

ETIOLOGY

Many suggestions have been made, but the etiology has been obscure since the first description of this lesion. The infrequent observation of the lesion in the male has suggested some peculiar predisposition in the female on possibly an anatomical or hormonal basis. Some authors[8] have suggested that previous pelvic inflammation, pelvic operations, pregnancies and pelvic injuries play no part in the cause, but Keen believed that a "Paracystitis" might be the cause of the primary lesion and stated that the ulcer is a secondary manifestation.[4]

Meads suggests that the interstitial cystitis with resulting fibrosis is the

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ultimate result of a neglected cystitis, just as chronic neglected urethritis may result in a stricture of the urethra.

related to the amount of available oxygen in a given tissue.

LeFur produced histologic ulcers by

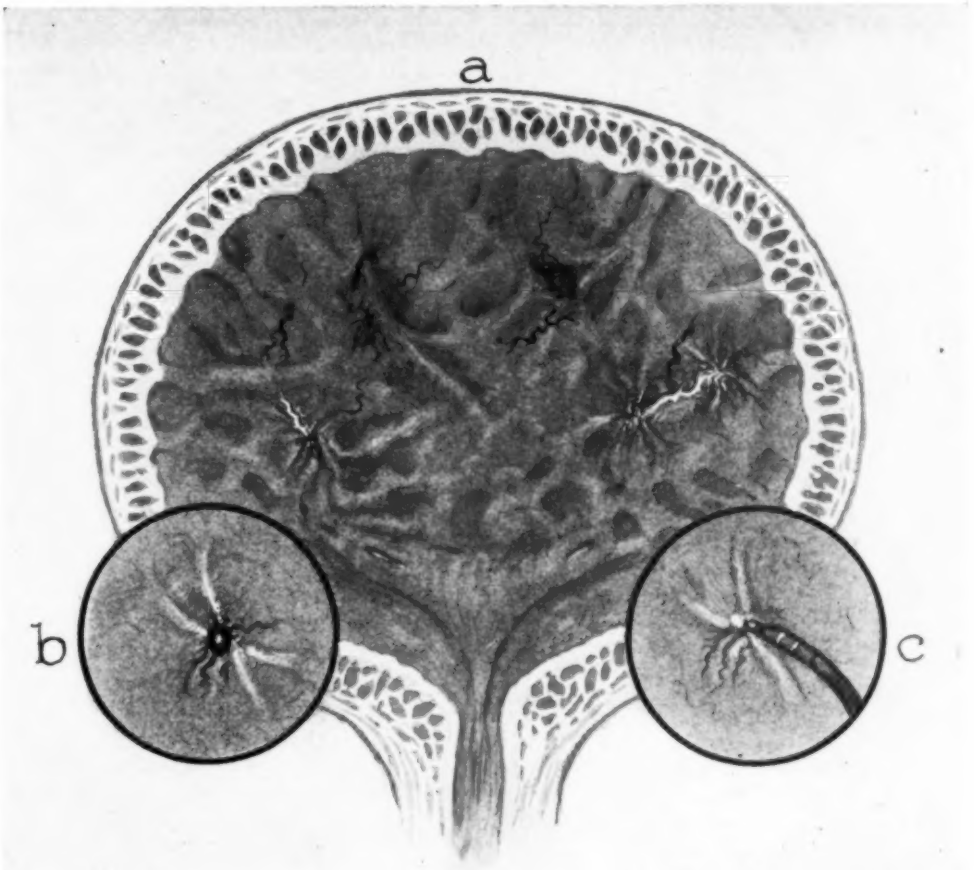

Fig. 1. a, Shows cystoscopic appearance of elusive ulcer during gradual distention of the bladder; cracking and bleeding at ends of the thin scar are demonstrated. b, The appearance of a droplet of blood from an elusive ulcer after overdistention of bladder. c, Application of fulgerating tip to and around ulcer bearing area.

Many authors, however, place great stress on the role played by foci of infection. Foremost among these is Rosenow who believes that he has produced an elusive ulcer in rabbits by simple intravenous injections of streptococci obtained from a dental abscess in a patient suffering from Hunner ulcer. He[9] has pointed out that streptococci of increased virulence are found to produce lesions in tissues in which the blood supply is high. This is well illustrated by the localization of virulent streptococci in such vascular organs as the kidney, lung and bladder. Localization and production of injury seem to be closely

inoculating blood with organisms and then injuring the bladder wall. But Hunner states that these ulcers did not resemble typical elusive ulcers.[19]

In his first discussion of the condition, Hunner suggested foci of infection such as the teeth, tonsils and the nasal accessory sinuses as a possible cause for the formation of the lesion. Infection of the cervix uteri because of its anatomical proximity to the bladder may also act as a focus of infection. The experiments of Winsbury-White clearly show the lymphatic connections between the bladder and the cervix. India ink, when injected into the cervix of a

guinea pig, was found to appear in the lymph spaces of the bladder wall, and likewise injections of tubercle bacilli into the cervix produced an inflammatory reaction in the bladder wall.[29]

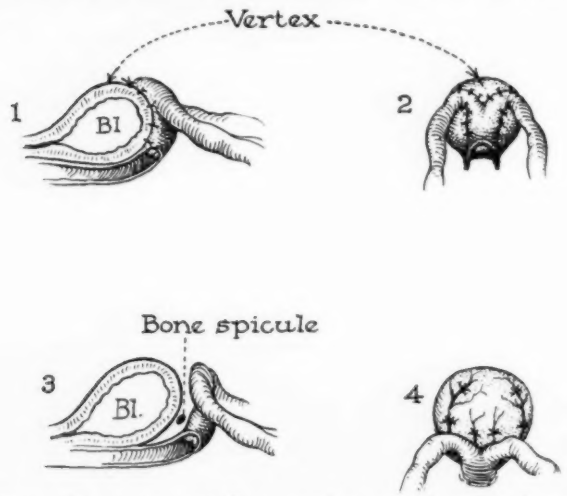

Fig. 2. Demonstrates the operative procedures on dogs. (1) Shows the vagina and uterine horns pulled up and sutured to vertex and posterior wall of bladder. (2) Same procedure but posterior view. (3) Shows method in which infected bone spicule was sutured in cul-de-sac between bladder and uterine horns. (4) Posterior wall and vertex of bladder showing the vessels which were ligated.

Dodson, in 1926, and Higgins, in 1930, both report an associated, dormant renal infection present in some of their cases of Hunner ulcer.[20,25] Meisser and Bumpus[8] believe the condition may be due to "focal infections harboring streptococci which have a selective affinity for the urinary tract." It is possible that this "selective affinity" for the bladder, in this instance, can be explained on a basis of lack of blood supply in cicatrized tissue. It is toward the production and evaluation of such localized areas of cicatrized tissue that the experimental work of this paper has been done.

HISTORY AND SYMPTOMS

The patient with this disease consults the physician complaining of the common but more exaggerated symptoms of "cystitis."

Frequency, both during the day and night, is always one of the major complaints. The desire to void is most urgent, it being most imperative that the sufferer immediately reach a suitable place for relief. The act is accompanied by strangury and pain of a sharp cutting character and may terminate with hematuria. The pain is not always confined to the bladder, but at times is referred along the urethra to the suprapubic area, the perineum, the rectum, and often to the inguinal region on the same side as the ulcer. When new ulcers form, the patient frequently is able to designate, by her symptoms, which side the new lesion is on. The irritability necessitates voiding every few minutes and is little alleviated by change in the reaction of the urine or lavage of the bladder. Rest at night is interrupted and the almost constant suffering of these victims, otherwise healthy, reduces them to the state of

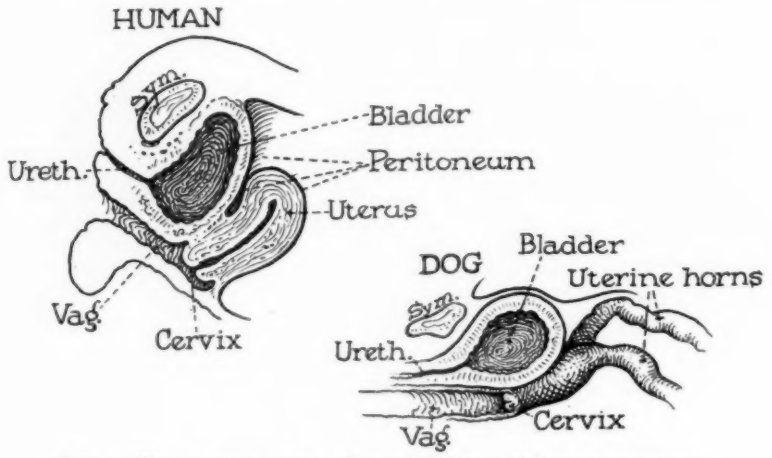

Fig. 3. Shows comparison of normal dog and human anatomy.

chronic invalidism and often nervous wrecks.

Frequently these individuals have suffered for years. They have run the gamut of doctors and have had their bladders lavaged with the then currently popular irrigating solutions, but all without permanent relief. In fact, nearly all of them have been subjected to some form of local treatment for "cystitis" without permanent relief. Many of them have been operated upon one or more times for various lesions without benefit.

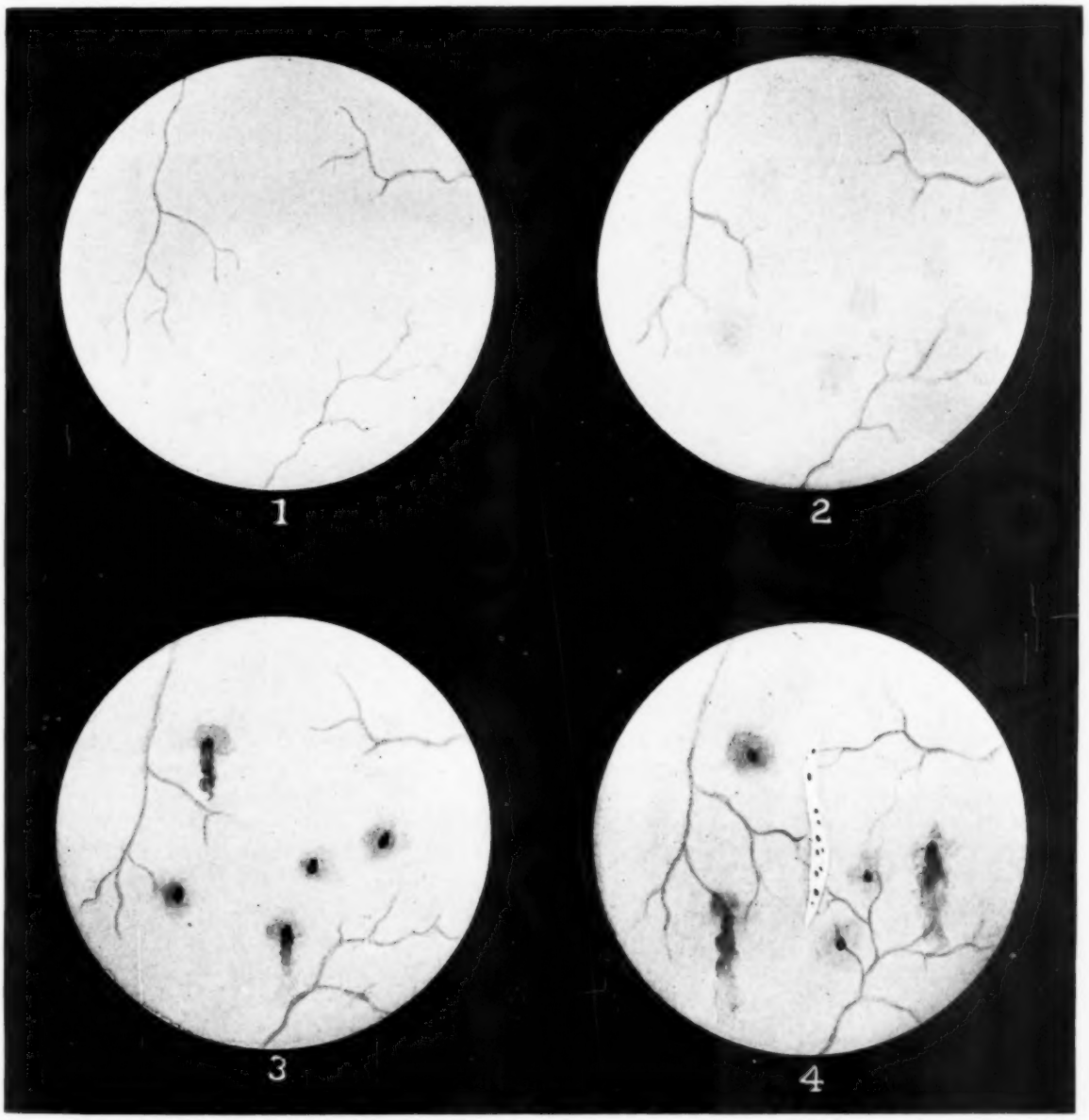

Fig. 4. Cystoscopic view of bladder of operated dog, showing development of petechial hemorrhages on gradual over-distention. (1) Ordinary distention; pale mucosa, faint vessels. (2) Increased distention; appearance of faint reddened areas. (3) Continued over-distention; areas become deep red and appear like small hematomas; vessels more pronounced. (4) Bleeding hematomas and splitting of mucosa.

DIAGNOSIS

The diagnosis of this condition is made on the basis of the history, urinalysis, cystoscopic and radiographic findings.

The victim of this disease, usually a woman in the middle decade of life,

(relatively few cases having been reported in men)[6] consults her physician because of increasing urinary frequency associated with marked vesical tenesmus, and occasionally terminal hematuria. In many cases, the bladder must be emptied every few minutes, with pain during, but more especially at end of urination. The distress is not confined to the day, but usually disturbs the sufferer at night to the same degree. Bumpus[10] is so emphatic as to state that "if symptoms are absent at night, the patient hasn't the disease." Occasionally there is a nocturnal exaggeration of the dysuria. We have seen individuals who would find it necessary to arise from ten to twelve times at night, being almost exhausted by the persistence of the discomfort.

The pain usually localized just above the symphysis pubis or to one or both sides of the midline, may be referred to the rectum, the perineal region, either or both hips and urethra. The severity of symptoms may vary in individuals, but are usually persistent and may be exaggerated by premenstrual pelvic congestion. Pelvic examination at any time will elicit the characteristic pain which is usually acute and sharp.

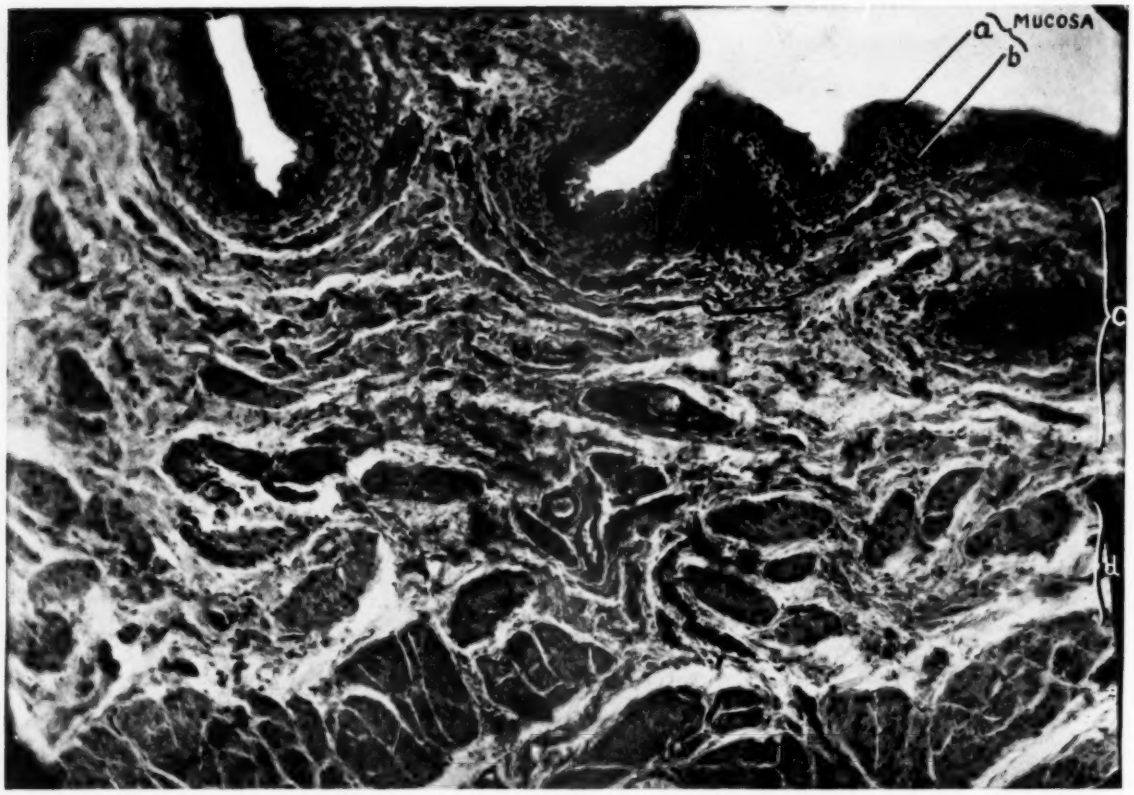

Fig. 5. Section from a normal dog showing a, epithelium, and b, stroma (of mucosa), c, submucosa or lamina propria, and d, muscle layer. Vessels are very small and lymhpoid tissue very sparse.

Macroscopically, the urine is usually sparkling clear. An occasional leucocyte and a few red blood cells may be found. Not infrequently it is necessary to centrifuge the urine to find the red cells. There is usually a marked increase in the number of red blood cells in the urine at the time of an exaggeration or exacerbation of symptoms. It is often only on these occasions that the patient is aware of gross hematuria. The finding of large numbers of white cells in the urine is not characteristic of this disease. Cultures of the urine are usually sterile.

The cystoscopic appearance is most consistent. The observer, having seen

one or more patients, will usually recognize the ulcer-bearing bladder. It should be pointed out, however, that it is not always possible, at the first cystoscopic examination, to distinguish the elusive ulcer when associated with a concurrent pyogenic cystitis. Treatment of this infection for a time with irrigations and rest often clears up the masking cystitis only to leave the persistent symptoms and cystoscopic picture of the elusive ulcer. (Fig. 1)

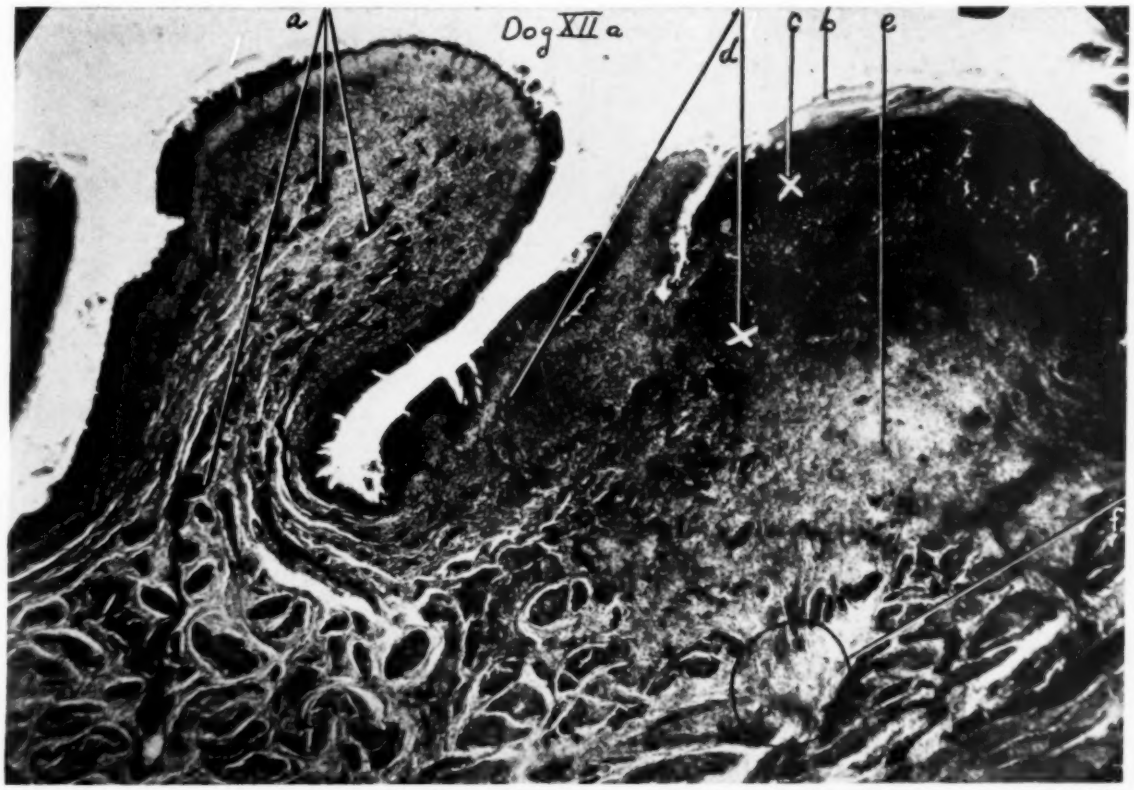

Fig. 6a. Very low magnification of bladder wall showing a, dilated capillaries of lamina propria; b, thin necrotic membrane replacing loss of epithelium; c, infiltration of round cells and p.m.n. leucocytes; d, areas of hemorrhage; e, area of edema; f, small accumulation of p.m.n. leucocytes (see high power). (From dog with ligated vessels of bladder wall. Duration ten weeks.)

To all intents, the bladder appears normal except for the ulcer-bearing area which is usually localized to the vertex. The bladder capacity is markedly reduced. A deep anesthesia is required for sufficient relaxation of the bladder to permit adequate distention for visualization of the ulcer in its true form. Many elusive ulcers of the bladder, are without a doubt, undiagnosed because the bladder is not distended under deep anesthesia. The usual sharp definition of the blood vessels is absent in the ulcer-bearing area and the normal glistening mucosa has assumed a diffuse dull red color. In the region of the involved mucosa, are seen one or possibly many grayish white, pale, elongated, slightly elevated ridges, varying usually from 1 to 2 mm. in diameter to 0.5 to 2 cm. in length, giving an appearance of scar tissue. These ridges may at times extend across the entire bladder wall in older cases. They are often seen to intersect. It is usually at these points of intersection that bleeding occurs, when the bladder is overdistended. The patient who has had the disease for a short time usually has short ridges and few, if any, are seen to cross. The ulcer is sometimes covered with a thin diaphonous film and upon the distention of the bladder, a crack develops, followed by the appearance of droplets of blood. Usually the bleeding

points appear as round droplets or beads, but occasionally are in a linear arrangement and the blood streaming from them

Fig. 6b. High power magnification of bladder wall showing, a, area of edema; b, a fibroblast; c, an accumulation of p.m.n. leucocytes; d, capillary with red cells.

gives a water-shed appearance. This picture is most characteristic if the distending fluid is not flowing into the bladder at the instant of observation. Not infrequently this picture is missed if the examination is made only while the water is flowing into the bladder. This cracking and bleeding upon overdistention of the bladder, is the most characteristic finding of the lesion. (In fact, this accounts occasionally for the red blood cells discovered at urinalysis.) Touching the ulcer with a catheter, fulgurating wire or probe, immediately produces bleeding and the characteristic sharp pain experienced by the patient when the bladder is overdistended. The bladder base, including the trigone and ureteral orifices, is practically normal in appearance. The ulcers are never seen on the trigone. Hypertrophy and elevation of the trigone is not uncommonly present as a result of bladder irritability. A small contracted and hypertrophied bladder often develops as a defense mechanism to pain on distention.

The radiographic findings demonstrated by cystogram are those of the small contracted bladder with the usual irregular border seen in this condition.

TREATMENT

Little more than temporary amelioration of the symptoms has been too often the result in the treatment of this affliction. Some cases will show periods of improvement for several weeks, often in no relation to treatment given.

Thorough overdistention of the bladder, under deep anesthesia (from 400 to 600 cc.), or until the ulcer cracks, offers most in the relief of symptoms. Prompt and complete relief of symptoms following simple distention is sometimes spectacular,

but frequently not permanent. Overdistention should be repeated at intervals depending on symptoms. Occasionally relief of short duration is experienced after direct application to the ulcer of such caustics as silver nitrate, silver iodide, or carbolic acid. Bladder lavage with 1 or 2 per cent solutions of carbolic acid at times will reduce the frequency and dysuria, but the relief is only temporary.

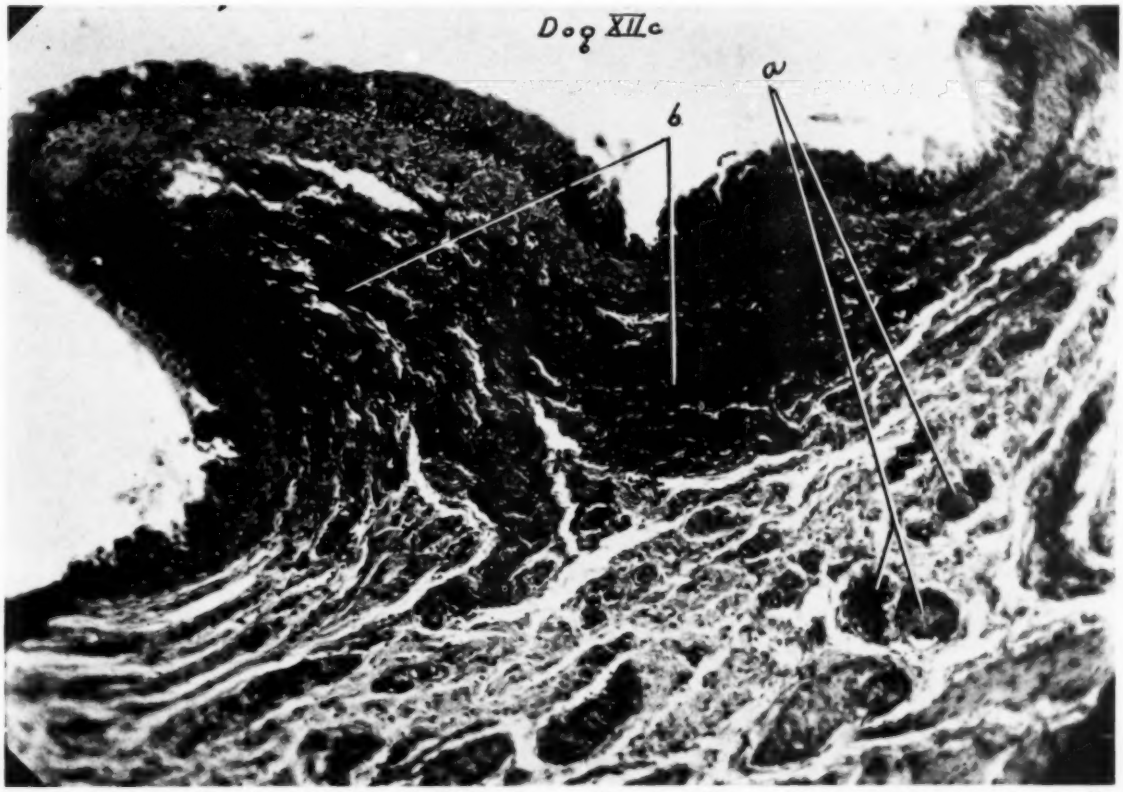

Fig. 6c. Low power section of bladder wall, showing, a, dilated capillaries; b, dense infiltration of red cells.

Intravesical application of ultraviolet light has been suggested;[11] however, nothing is mentioned in the literature as to its efficacy. Very early, Hunner came to the conclusion that "no form of treatment will suffice, except complete excision of the inflammatory area." He advocated wide excision of the ulcer and the edematous bladder wall, and attributed recurrence after resection to incomplete removal of the involved bladder wall. Keen also suggested the excision of the diseased area, "the limits of the excision to be determined not by ulcerations, but by the distinctly outlined edema." Very often, however, the procedure so limits the bladder capacity as to leave the patient in about as deplorable a state as before in so far as her frequency is concerned, but it may give relief from the pain. Frequently recurrences have occurred following even extensive resections of the bladder, so that this method of treatment has largely been abandoned.

In recent years, the introduction of high frequency electricity to the urologist's armamentarium, has been an aid in controlling these ulcers. Where the ulcers are single, fulguration through the cystoscope may give prompt relief. Very often following overdistention, supplemented by fulguration (or electro-coagulation) the symptoms immediately disappear, the patient is removed from her virtual invalidism and can return to normal activity. Unfortunately, too often there are several ulcers requiring many and repeated dilatations and fulgurations. Very frequently this combination of treatment must be repeated

at intervals of three to six months. This procedure in no way prevents recurrence.

Pieri[11] was first to point out the possibility of relieving the pain in the bladder that all vesical pain can be controlled by presacral neurectomy, and that the operation is one to be resorted to only in more extreme cases.

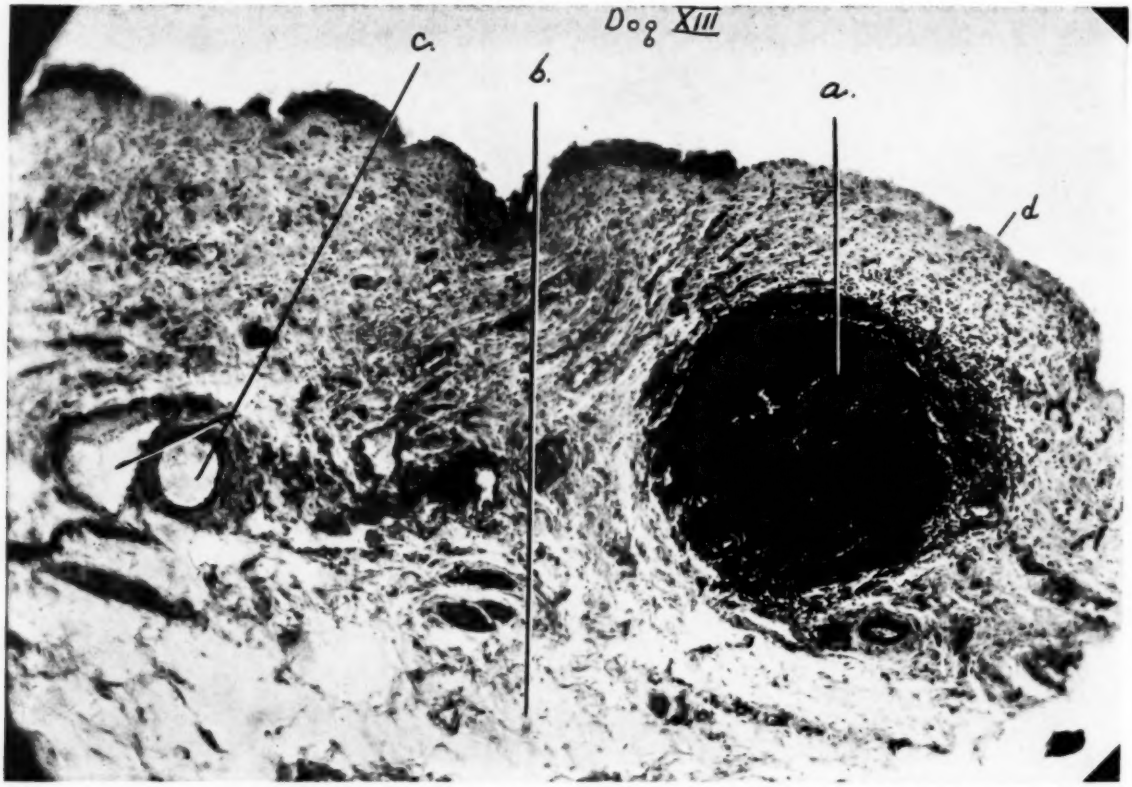

Fig. 7. Low power section of bladder wall showing, a, dense hyperplasia of round cells; b, separation of fibers of lamina propria, probably artifact; c, dilated vessels; d, epithelium lost in preparation of slides. (From dog with ligated vessels. Duration twelve weeks.)

lesions by section of the presacral nerve. In 1926 he performed the operation to relieve the distress from painful cystitis. Vianncy reported another case the following year. In 1931, Learmonth[12] made a preliminary report on four cases of this class. Three were suffering from a Hunner ulcer, the fourth from intractable pain due to tuberculous cystitis persisting nine years after nephrectomy. In a subsequent communication[13] he reported a satisfactory result in six out of eleven cases and notes no difference in the results between simple presacral neurectomy and that after the more extensive operation devised by Pieri which aims at interruption of all possible pathways from the bladder to the central nervous system. The work of Foulds[14] and others, demonstrated that it cannot be claimed

Bilateral transplantation of the ureters into the sigmoid has been resorted to by Counseller[15] in severe cases with satisfactory results, but is overshadowed by the operative mortality of 23 per cent.

Sebening,[16] in experiments on dogs, successfully engrafted an isolated loop of small intestine on the dome of the bladder and thereby increased the capacity of the latter organ. He states that he successfully applied this method to the treatment of patients whose bladders had been contracted by infection. He believes it is indicated where there are poor rectal sphincters, making it inadvisable to transplant the ureters to the pelvic portion of the colon.

Folsom and O'Brien,[17] following the work of Alexander and Christie,[18] have

recently reported their observations on seven cases in which they injected absolnte alcohol. They were impressed by the prompt relief their patients have experienced. Under gas anesthesia, and using a long flexible needle through a McCarthy panendoscope, they injected absolute alcohol by multiple punctures directly into and about the ulcers. Adequate time has not elapsed to determine the duration of the period of relief. They feel that the procedure is entirely free from danger, provided care is exercised to prevent rupture of the bladder from overdistention.

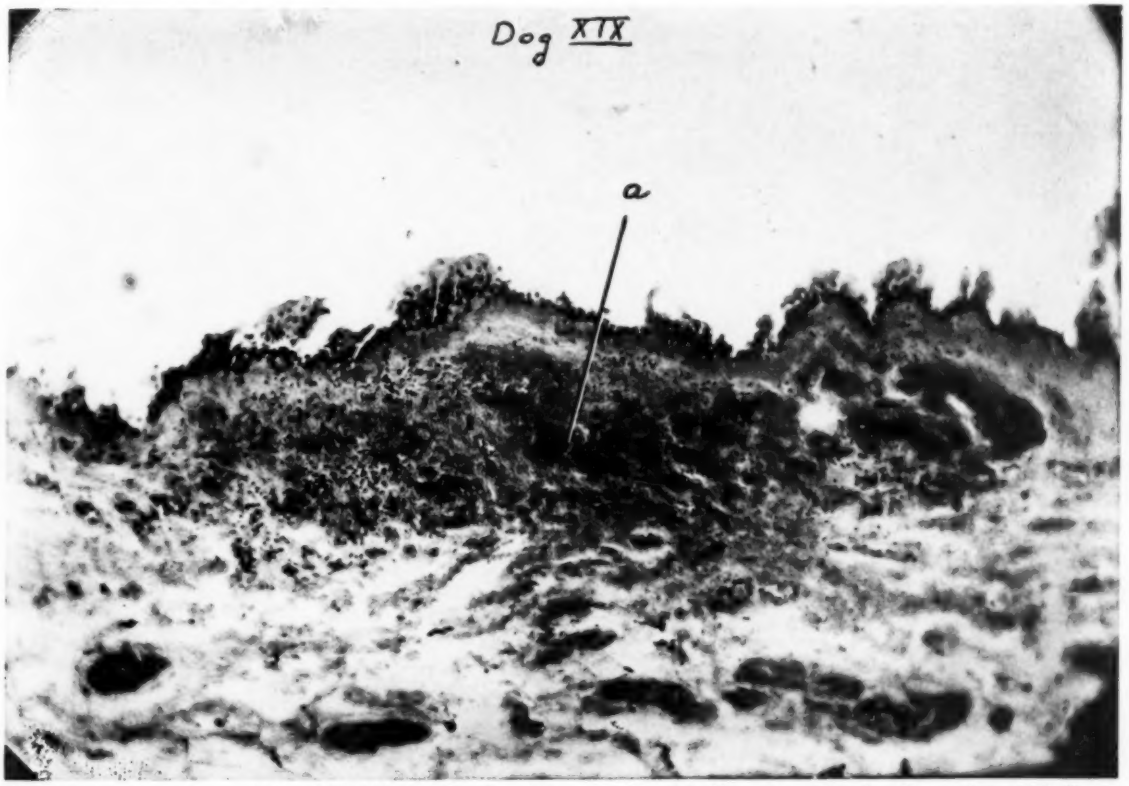

Fig. 8. Low power, section of bladder wall, showing, a, area of infiltration of red cells under epithelium. (Following over-distention of bladder subjected to infection from without. Duration seven weeks.)

Recently, George M. Fister[30] reported marked improvement in symptoms in an elusive ulcer patient following intravenous injection of gold sodium thiosulphate and intramuscular injection of bismuth, the treatment being based on the apparent similarity in the histopathology of elusive ulcer and lupus erythematosa.

The great variation in treatment of elusive ulcer of the bladder may be explained by the fact that none is as yet adequate as far as permanency is concerned. Meads attributes this variation of results of treatment to the fact that he believes there are three stages of these ulcers. If the ulcer is fulgurated in the first two (inflammatory) stages spectacular results may be obtained, while treatment during the third (or stage of marked scarification) gives very discouraging results.[24]

In the light of what has been suggested concerning the etiology of this disease, it is probably well to remove all foci of infection in addition to attempting to obliterate the ulcer.

However, thorough and faithful overdistention of the bladder under deep anesthesia, supplemented by cystoscopic fulguration, offers much in the therapy of this disease.

PATHOLOGY

It is by this time clear that the theories concerning the etiology of elusive ulcer

supported by very thorough experimental work, are almost as numerous as the authors propounding them. We believe with Meads that, when one has completed a review of the literature on the subject, one is almost where Hunner left him in 1914.

In attempting this experiment, we hoped to be able to shed some light on the vague etiology of this condition. There seems to be some cause for encouragement along the lines of procedure we have been using. The success of the experiment obviously depends on two factors: reproduction of the cystoscopic picture, already described, and second, reproduction of the histopathologic picture.

Hunner's description of the histology is still representative of the consensus of opinion, and is mentioned for the purpose of comparison with our own histologic findings. Hunner states that the histologic picture of all operative specimens is uniform, being one of chronic inflammation involving all coats of the bladder, but being localized to the thickened or involved area. At the site of the minute ulcer, there is loss of epithelium and granulation tissue is seen in the underlying mucosa. The mucosa shows a preponderance of connective tissue and infiltration of small round cells, and leucocytes. The transitional type of epithelium has changed to a flattened type. The capillaries in the mucosa in the neighborhood of the ulcer are abundant and filled with leucocytes. There are also some enlarged lymph spaces. A thick basement membrane is a prominent feature. The muscularis is hypertrophied and shows enlarged lymph spaces filled with small round cells. "*The peritoneum subtending the diseased area shows decided thickening.*"[21] Higgins adds that the bladder wall is thickened by edema and fibrous tissue proliferation, plasma cells and areas of round cell infiltration are quite marked in non-ulcerated areas beneath basement membrane and in the submucosa of ulcerated areas there is an infiltration of polymorphonuclear leucocytes. He states that the mucous membrane over the lesion may be broken or it may be merely edematous. "Occasionally the inflammatory process may extend beyond the confines of the bladder wall and involve the paravesical tissues and adjacent peritoneum. *In these cases adhesions exist between these structures and the bladder wall.*"[25]

The ulcers are small and may be multiple. They are found on the lateral walls. They are never found on the trigone. The ulcers are only seen on overdistending the bladder. Their bases are very red. Very small engorged vessels are seen radiating away from them giving an appearance of a pinkish halo around a darker ulcer. The ulcers are more or less circular, but at times have a linear form as the result of a previous distention of the bladder which has cracked the mucosa above the rigid area of localized intramural cystitis. These cracks may form thin linear scars, or the overlying mucosa may heal and the ulcer will not be seen at the next examination.

Wehrbein describes a similar picture calling attention to the presence of lymph follicles scattered throughout the submucosa.[26] We believe that the sequence of events in the production of a Hunner ulcer as hypothesized by Meads deserves mention. They are as follows: "chronic cystitis, resulting fibrosis, contraction of bladder, avascularity, atrophic mucosa, and finally ulcer in the least vascular portion, namely the apex of the bladder. The contracted bladder, a condition analogous to stricture of the urethra, is the end result."[24] Hunner believes that the location of these lesions in the vertex or free portion of the bladder, instead of the base where there is a richer blood and lymph supply probably argues against the focal infection theory. On the associated pathology of this condition very little is described, the usual Hunner ulcer being thought to exist in the presence of an otherwise quite normal urinary tract.

EXPERIMENTAL WORK

Our experiments have been confined to an attempt to produce a Hunner ulcer-like lesion in the posterior bladder wall. The following methods were used: (Fig. 2)

1. Simple ligation of vessels of the posterior wall and vertex of the bladder from external or peritoneal aspect.

2. Suturing of the vagina and uterine horns to the posterior wall and vertex of the bladder.

3. The bladder wall was scraped with scalpel to promote formation of adhesions between bladder, vagina, uterus, and omentum.

4. Introduction of an infected bone spicule in a cul-de-sac, formed by suturing posterior bladder wall to the uterine horns using the fat of the uterine horns to close in the pocket at the sides and vertex. These bone spicules were infected with streptococcus viridans taken from a tooth abscess of a patient who was *not* an elusive ulcer patient.

TABLE I

RESULTS OF DOG EXPERIMENTS

Dog	Operation	Cystoscopy Findings	Duration of Experiment	Gross Pathology	Histology
V	Jan. 22: Posterior wall of bladder scarified and sewed to vagina. Apr. 20: Infected bone spicule sewed in left Fallopian tube and uterus. See Fig. 2.	March 15: Cystoscoped and bladder distended. Mucosa is seen to split in long striae along posterior bladder wall. Apr. 2: Bladder overdistended. No gross cracks produced but a few small hemorrhagic spots are seen on the posterior wall.	61 days. Died Apr. 22.	Phelgmon of left posterior bladder wall. Dense adhesions between vagina and bladder. All sections are made from the post. wall and vertex of bladder.	The bladder wall immediately adjacent to uterus shows changes of edema and extravasation of red cells, but no infiltration of p.m.n. leucocytes. Vessels of lamina propria are dilated and conjested. There is no edema and only slight increase in round cell infiltration in lamina propria and none in mucosa.
IX	Feb. 19: Three vessels of posterior bladder wall ligated. Apex and post wall of bladder sewed to vagina and uterine horns. (Bladder and vagina scarified.)	Apr. 2: Bladder overdistended. It has the appearance of normal bladder. April 21: On overdistending the bladder there appear 12 petechial hematomas on left posterior bladder wall. Irrigating water returns red following distention. Further distention produces one large split (1 cm.) in the mucosa (midline of post. wall). See Fig. 4. May 24: Moderate dilatation produces multiple petechial hemorrhages on posterior wall of bladder. Anterior wall and vertex of bladder normal. A few of the petechial spots are in center of a small hematoma under the epithelium. June 24: On posterior wall and right side of bladder there are present about 7 faint lines. They appear like fine trabeculae or linear scars. There are faint hemorrhagic spots along each one following distention. Irrigating water is pink. Bladder capacity decreased.	17 wks. Died June 24.	Posterior bladder wall adhered to uterus in only 2 small areas at vertex. Otherwise free of adhesions.	Fibrils of lamina propria separated by edema. Very few p.m.n leucocytes are seen. One section shows 2 small patches of round cells beneath the epithelium. No hemorrhage present.

Our reasons for these procedures were as follows:

A. It is known that this condition is one largely seen in women. This leads us among other things to a consideration of the anatomical relationship of the female genital organs, especially those adjacent

to the bladder. These are from the vertex down to the trigone, respectively: fundus uteri, cervix uteri, and vagina, the vagina being adherent to the posterior wall of the bladder by dense fibrous tissue; the cervix by loose connective tissue, and of the bladder often extending to the peritoneum."[21]

D. A number of our ulcer patients gave a history of bladder symptoms definitely occurring three or four months following pelvic operations.

TABLE II

Dog	Operation	Cystoscopy Findings	Duration of Experiment	Gross Pathology	Histology
X	Feb. 25: 6 vessels of posterior bladder wall and vertex ligated.	May 20: Bladder appears normal. Continuous overdistention under deep anesthesia produces small hematomas on posterior bladder wall above trigone only (appears like scraped skin.) June 24: Crystalline deposits seen on posterior bladder wall. There are also present 3 hemorrhagic patches on posterior wall which become deeper on overdistention. Bladder capacity small. No bleeding.	16 wks. Died June 24	Dense adhesions between vagina, omentum and posterior bladder wall.	There is a limited number of hemorrhages in lamina propria. Its fibrils are separated by edema. There is a diffuse and light scattering of p.m.n. leucocytes and round cells of equal numbers in lamina propria. There is some thickening of bladder wall.
XI	Mar. 8: Posterior bladder wall and apex scarified and sewed to vagina and uterine horns. 3 vessels of apex of bladder ligated.	May 20: Overdistention produces multiple small reddened areas on (posterior wall?). Return flow pink. June 25: Overdistention produces small petechial hemorrhages on posterior bladder wall. There is a split in the mucosa at apex of bladder	14 wks. Died June 25	Dense adhesions between bladder and uterus.	In the lamina propria are small aggregations of small round cells and plasma cells. There are large macrophages filled with yellow pigment giving evidence of old hemorrhage. There are few accumulations of red cells under the epithelium.
XII	Mar. 10: Posterior bladder wall and apex scarified and sewed to uterus. Two large vessels of posterior bladder ligated.	May 22: Bladder mucosa white. Capacity only 20 cc. Small petechial hemorrhages seen throughout the bladder wall following continued distention. Return flow bloody.	10 wks. Died May 23	Very loose adhesions between bladder and vagina.	In one area, the epithelium is absent, and is replaced by a thin layer of necrotic material which overlies a massive infiltration of both p.m.n. leucocytes and small round cells. In the deeper layers, there is an extravasation of red cells and edema. A few young fibroblasts are seen here. In one area muscle fibrils are swelled by edema. There is a congestion of capillaries in lamina propria which is thickened 2x normal. There is a scattered infiltration composed equally of round cells, plasma cells and p.m.n. leucocytes in deeper layers of lamina propria. See photo micrographs, Figs. 6(A) 6(B) and 6(C).

the fundus uteri resting on the vertex of the bladder, and separated from it by two layers of peritoneum. (Fig. 3.)

B. Almost all these lesions appear on the posterior wall of the vertex of the bladder.

C. The pathological picture of an elusive ulcer is one that involves "all the coats

E. The urine is sparkling clear and negative on cell count and culture and remains so even after repeated cracking and opening of the ulcer. This fact leads one to believe that a focus of infection may not necessarily be a part of the picture. The above evidence strengthens our contention that localized small cicatricial

areas on the posterior bladder wall whether produced by surgical adhesions, pelvic inflammation, vessel ligation, or hematogenous infection, may develop into lesions similar to the ulcer of Hunner.

However, it must be remembered that these localized cicatricial areas because of their avascularity are areas of decreased tissue resistance and may be subject to a hematogenous infection. How an infection from a distant focus would effect the small cicatrized area, we will not be able to fully evaluate. We have observed the effect of infection for only two months. Therefore, this experiment will concern itself with the simple production of cicatricial areas of posterior bladder wall as described above and the observation of the cystoscopic and histologic picture.

TABLE III

Dog	Operation	Cystoscopy Findings	Duration of Experiment	Gross Pathology	Histology
XIII	Mar. 22: 2 large vessels on post. wall of bladder and 5 vessels on apex ligated. Bladder wall then approximated to vagina and uterus.	May 22: Yellowish encrustation seen on trigone. Following distention of bladder, a hematoma developed in the mucosa under the encrustation. Posterior wall and vertex of bladder small petechial hemorrhages were seen. Good capacity of bladder. June 24: Bladder capacity very small. Only one area of 2–3 petechial hemorrhages seen on upper aspect of post. wall. Return flow bloody after prolonged distention.	12 wks. Died June 24	Dense adhesions between posterior wall and apex of bladder, vagina and omentum.	There are similar, but less extensive changes as in Dog XII. There are several concentrated collections of small round cells in lamina propria. Elsewhere in sections, infiltrating cells are few. Hemorrhage involves mucosa in a few areas. See photomicrograph Fig. 7.
XV	Apr. 27: Bone spicule soaked in 24 hr. culture of strep. viridans sewed in between bladder and vagina.	May 24: Trigone of bladder had a scraped appearance. A small petechial hemorrhage appears on distention, on trigone only.	7 wks. Died June 21	Dense adhesions between bladder and vagina. (Sm. contracted bladder.)	Bladder wall thickened. No hemorrhage is seen. Slight changes observed in mucosa or lamina propria. Thickening occurs in outer layer of bladder wall adajcent to the infection.
XVI	Apr. 29: Infected bone spicule sewed in between bladder and vagina. Bladder and vagina scarified.		3 wks. Died May 19	Dense adhesions between bladder, vagina and uterine horns.	Bladder wall thickened. Increased amount of capillaries in mucosa, otherwise not much change. No hemorrhage seen.
XIX	May 5: Bladder scarified and infected bone spicule sewed in between the bladder and vagina.	June 25: Distention of bladder produces 3 small hematomas of mucosa. No gross bleeding is seen, but return flow is bloody.	7 wks. Died June 25	Loose adhesions between bladder wall and vagina.	The principal change is numerous extravasation of red cells in lamina propria beneath the epithelium. There are a few similar extravasations between muscle bundles. See photo micrograph Fig. 8.
XX	May 5: Vessels of posterior bladder wall and vertex ligated.	June 25: Normal bladder. Good capacity.	7 wks. Died June 25	No adhesions between bladder wall and other organs. Post. wall of bladder appears shrunken between areas of ligated vessels.	Not much change seen microscopically. No indications of even a slight hemorrhage.

SUMMARY AND COMPARISON OF CYSTOSCOPIC FINDINGS IN EXPERIMENTAL DOGS

(Fig. 4.) Cystoscopically, the bladders had a similar picture, whether adhesions were produced by infection or trauma, or whether vessels were ligated. The mucosa

in the involved area, in most cases, was pale with a faint demarcation of vessel before overdistention of the bladder. On overdistention of the bladder the mucosa would assume a deeper reddish tint and many petechial hematomas would appear. Occasionally, these would become minute hemorrhagic spots. Often after prolonged distention, the mucosa of the posterior bladder wall would split, in striae from 1 to 4 cm. long.

The urine was usually very clear before distention and tinged pink or red after distention. The bladder capacity of almost all dogs was decreased. These petechial hemorrhages were usually more marked in those dogs which we had observed for a longer time and were slightly more numerous in bladders where some of the vessels of the vertex were ligated.

A few of the dogs evidenced pain by groaning when their bladders were overdistended even under deep anesthesia of intravenous nembutal. Normal dogs, however, when subjected to overdistention of the bladder with the same hydrostatic pressure, and some degree of anesthesia, gave no evidence of pain. There was also no indication of splitting or hemorrhage in the mucosa or of discoloration of distending fluid in these normal dogs.

Summary and Comparison of Gross Pathology in Experimental Dogs. A series of fifteen dogs were used for the experiment, but the last four dogs showed no cystoscopic changes after only six weeks, so were not sacrificed for this report. The bladders of eleven dogs and 120 microscopic slides were submitted for examination. Dense adhesions formed between the posterior bladder wall, uterus and vagina in almost all dogs. Especially was this true of dogs where infection was introduced against the posterior bladder wall. A more typical cystoscopic and histologic lesion was produced, however, in dogs whose bladder vessels were ligated, even in the absence of dense adhesions.

Summary and Comparison of Histopathology in Experimental Dogs. (See photomicrographs, Figs. 5, 6, 7, and 8. Also Tables I, II, III, and IV.) Many of the sections show a picture of chronic inflammatory change. There is a hyperplasia of lymphatic tissue either as a scattered infiltration of round cells or in the form of small lymphoid follicles in the mucosa and lamina propria.

TABLE IV

Dog	Operation	Cystoscopy Findings	Duration of Experiment	Gross Pathology	Histology
XXI	May 11: Vessels of posterior wall and apex of bladder ligated. Bladder wall scarified. Infected bone spicule inserted between bladder and vagina.	June 24: Good capacity. Normal appearance. Only one area over left posterior bladder wall shows small petechial hematomas, on overdistention. Irrigation water is pink.	6⅓ wks. Died June 24	Dense adhesions between entire posterior wall and apex of bladder, vagina and omentum.	Epithelium is thinned out in one place. There are localized areas of extravasation of red cells. The bladder wall is thickened. The capillaries in lamina propria are numerous and distended with red cells. There is edema of lamina propria. There is no cellular infiltration.

In many slides, there are small hemorrhages in the mucosa beneath the epithelium, and occasionally in the lamina propria. This hemorrhage occurred in dogs who were cystoscoped and overdistended immediately before the bladders were removed. However, hemorrhage into the tissues did not occur in dogs who had not developed some adhesions between the bladder and adnexa.

Increased thickness of the lamina propria or submucosa was slightly more marked in bladders where the vessels had been ligated. These bladders also had more marked infiltration of round cells, plasma cells, and polymorphonuclear leucocytes.

The histologic involvement of the bladders whose posterior walls were infected

was practically all confined to the outer coats of the bladder adjacent to the infection, very little changes being observed in the mucosa and lamina propria.

SUMMARY

1. A summary of the literature on elusive ulcer of the bladder is offered.

2. An experimental study has been carried out in an attempt to determine the etiology of elusive ulcer. Dogs were used as experimental animals.

3. Experimental lesions have been produced in the bladders of dogs which resemble elusive ulcers both cystoscopically and histologically.

4. It is a question whether a more typical lesion would be produced if the duration of the experiments were prolonged. The difference between the human and dog anatomy may be a factor in explaining the occasional difference in the cystoscopic appearance.

We wish to express appreciation to Dr. Carl Apfelbach and his pathology department of the Presbyterian Hospital for their cooperation in the preparation of all microscopic sections used in this experiment.

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THE UROLOGICAL COMPLICATIONS OF CARCINOMA OF THE CERVIX*

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THERE has been, until recently, a general lack of recognition of the fact that pathological changes in the urinary system are common complications of carcinoma of the cervix, either as a direct result of extension of the disease or as sequelae of its treatment. Faerber, Herger and Schreiner, Colby, Schmitz, Martin and Rogers and others, have published excellent papers on the subject and all have stressed the paramount importance of urological study in cases of cervix malignancy. In previous communications, the authors have described the frequent involvement of the urinary bladder and they have stressed the high incidence of ureteral obstruction in a large series of cases studied clinically and at post-mortem examination with reference to changes in the upper urinary tract. Reference is made to these reports for a detailed discussion of this subject. Our original material was drawn from 683 cases of carcinoma of the cervix admitted to the Pondville Hospital (Massachusetts Department of Public Health) since 1927, 257 of which were investigated urologically in some detail. Since the publication of these papers we have examined 133 additional cases.

Before discussing the urinary tract complications of the disease, it is essential that we be cognizant of its character and the pathways of its extension. Carcinoma of the cervix may spread upward and laterally into the parametrium, anteriorly toward the bladder, and posteriorly toward the rectum. It very frequently extends along the vaginal wall. The spread of the lesion depends in some degree on the nature of the growth. Three general types are recognized; the proliferative, ulcerative, and invertive. The proliferative (fungating or cauliflower) group is often bulky in character and frequently of low-grade malignancy. Its bulk may give some protection to the bladder during irradiation and it may present the picture of extravesical pressure on bladder inspection. The invertive (endocervical) type remains confined to the cervix for a relatively long time before invading the bladder or extending into the broad ligament area. The ulcerative type is in most cases of high malignancy and has a greater tendency to bladder invasion and fistula formation. A classification of the malignant process as regards extent of disease is also of the utmost importance in this discussion. Group A is that in which the carcinoma is confined to the cervix. Group B is that in which there is uterine cavity or vaginal wall involvement. Group C includes those cases which have disease extension to the broad ligaments, and Group D those in which there is wide fixation of the pelvis or even remote metastases. Obviously, involvement of the urinary organs is more frequent in the C and D groups and it is also true that the detection of such involvement by cystoscopy, sometimes leads to more accurate classification than is possible by pelvic examination alone.

The failure to recognize the presence of urinary tract pathology in this disease is due in many instances to the absence of symptoms referable to the bladder or upper urinary organs. Definite bladder involvement and advanced renal damage may take place without disturbances sufficiently marked to attract attention. Urinary frequency is the most common bladder symptom, but with the advent of infec-

* From the Urological and Gynecological Clinics of the Pondville Hospital (Massachusetts Department of Public Health).

tion, extravesical pressure or actual malignant invasion, dysuria and urgency may develop. Incontinence, partial or complete,

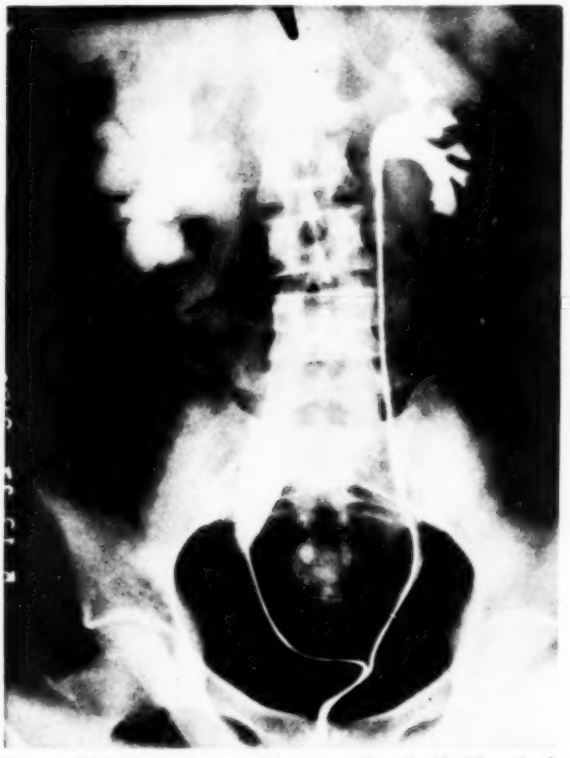

Fig. 1. Photograph of pyelograms, Pondville Hospital, No. 2103. Case of woman, age 52, who had radium treatment for carcinoma of the cervix in April, 1930, and a right nephrectomy in June, 1937. There is no present evidence of active malignant disease in the cervix. Note the extreme hydroureter and hydronephrosis resulting from ureteral occlusion on the right side.

suggests the possible development of vesicovaginal fistula, although distortion of the bladder floor and sphincter by the encroaching tumor may be a factor in faulty control. The most distressing symptoms that we have encountered are referable to the upper urinary tract and are those of ureteral obstruction and renal insufficiency.

Inspection of the bladder was carried out in 238 cases of our series. It is a procedure of great value both in prognosis and in the accurate grouping of the malignant neoplasm. The initial indication of direct vesical disturbance by the tumor presents itself as a distortion from extra-vesical pressure. It is without question the most common bladder abnormality found by cystoscopy in this disease. The authors have described it as presenting the picture, . . . "usually of a uniform elevation of

Fig. 2. Photograph of specimen removed in case described in Fig. 1.

the proximal trigone and posterior wall covered with normal mucosa and unaffected by distention. It may resemble the ordinary uterine eminence seen so often in the female bladder floor, or may be so accentuated as to form deep lateral sulci on each side." The picture must be correlated with the pelvic findings, of course, to be certain that it results from tumor. Localized areas of increased vascularity, mucosal hemorrhage, and edema, suggest imminent bladder wall invasion or actual

involvement. It is probable that extravesical pressure associated with edema connotes actual malignant disease in the bladder wall. In more advanced cases, one may see submucosal nodules or definite neoplasm projecting into the bladder cavity. The end stage of this whole process lies in the development of a vesico-vaginal fistula, though in its earliest stages the opening may be so minute that clinical or cystoscopic recognition is impossible.

A most important bladder complication of carcinoma of the cervix is one which results from the treatment of the malignant disease rather than from the disease itself—the so-called "remote radium reaction." This must be distinguished from the transient early or acute reaction which occurs at the height of the radiation effect in the cervix. The late reaction presents itself many months or even years after treatment, and is due to vascular changes varying from a mild endarteritis to a complete ischemic necrosis. The bladder picture may be very characteristic and present a sharply defined area of central slough surrounded by a zone of hyperemia and edema located in the posterior midline just above the trigone. However, the picture may vary from a small area of congestion to definite ulceration and slough, and its location in the bladder depends on the region of maximum radiation effect. The development of fistula from the effect of radiation rather than from disease itself is not common. The symptoms of the late radiation reaction are the triad of frequency, dysuria, and hematuria, which in most instances appear acutely without a previous urinary history, long after radium treatment directed to the cervix. The clinical distinction between this entity and actual vesical invasion by tumor, frequently taxes the diagnostic acumen of the most brilliant cystoscopist. A definite diagnosis can be made only by a correlation between the bladder picture and the status of the disease in the pelvis, and by repeated observations of the bladder relative to regression and progression of the lesion. Biopsy may be justifiable at times. The prognosis as regards healing is good in most cases.

Due to the anatomical proximity of the distal ureters to the broad ligament regions and the anterior vaginal wall, their involvement as the disease progresses would be expected. Warren has stated that the most common cause of death in this disease is the impairment of renal function due to ureteral occlusion, and Ewing has written that the natural termination of most cases of uterine cancer is through uremia from occlusion of the ureters. The silent death of a kidney is not uncommon.

In most cases, the encroaching tumor itself is the direct cause of the ureteral occlusion, although inflammation and edema in the region of the tumor may exert the first effect. Actual compression by growth is followed, as the lesion advances, by invasion of the ureteral wall and lumen. In quiescent or cured cases, fibrosis alone may be the cause of the stenosis. It is probably true also that irradiation, either by X-ray or radium, may precipitate complete ureteral obstruction through edema, where previous partial occlusion has been present. We are of this opinion because we have encountered cases in which anuria has occurred so soon after treatment that there has seemed to be no other reasonable explanation for its occurrence.

In the writers' original series, in which 174 cases were investigated urologically or by post-mortem study, 123, or 70.7 per cent, showed positive signs of ureteral obstruction; 46 were Class C, and 77 were Class D cases, showing, as might be expected, that the incidence of ureteral involvement varies in direct ratio with the extent of the disease.

In view of the established frequency of urological complications, we are subjecting all cases of malignant disease of the cervix at the Pondville Hospital and those encountered through consultation in private practice to cystoscopic study when they are first seen, and before treatment is instituted, so that bladder involvement or

interference with ureteral drainage will be recognized promptly. It is true that the investigation of most of the Group A and B cases will reveal no evidence of urological disease, but even in such cases we have a baseline for comparison with later observations as the disease advances. In the study of all cases specific questioning of the patient is important, with reference to symptoms which may signal bladder involvement or ureteral occlusion with resulting renal impairment. The routine physical examination may fail to detect these changes. Determination of renal values by the 'phthalein function test and estimations of blood chemistry are of great importance, although kidney damage is earliest and best detected by the former. We have found in many instances that the blood nitrogen level may remain within normal limits until the very late stages of the disease, while the 'phthalein excretion is low or absent.

Routine inspection of the bladder and urethra should be carried out to determine the presence or absence of local tumor invasion, fistula, or radiation reaction. At times, urethral involvement with obstruction may be encountered as the disease spreads from the vaginal wall. It should be emphasized that a negative bladder picture, and ureteral orifices normal in appearance, does not exclude the possibility of serious ureteral occlusion. Catheterization of the ureters, if possible, should be routine. Obstruction, when present, may vary in degree from complete stenosis to lesser grades of narrowing. When resistance to the catheter, or obstruction, is encountered, it is usually at a point 4–6 cm. above the bladder where the ureter lies beneath the broad ligament and adjacent to the cervix.

Ureteral catheter specimens of urine should be examined microscopically and bacteriologically because the presence or absence of infection bears heavily on the whole problem of the blocked kidney. An asymptomatic obstruction with the advent of infection may become clinically evident through chills, fever, and localized pain. If ureteral catheterization cannot be carried out, indigocarmin may be used to ascertain the renal values or to assist in the identification of the ureteral openings in difficult cases. It should be noted that easy catheterization with catheters of ordinary size does not preclude the possibility of obstructive changes in the ureter and renal pelvis.

Visualization of the kidney and ureter by X-ray studies, and especially by retrograde uretero-pyelograms, reveals better than in any other way the degree and extent of ureteral dilatation. In those cases where the ureters cannot be catheterized, intravenous urography is of great value, but the information derived by this method is less conclusive as a rule.

For the treatment of patients with ureteral occlusion, we have at our disposal ureteral dilatation, nephrostomy, nephrectomy and ureterostomy, and ureterointestinal anastamosis, in addition to the general program of medical measures directed to the improvement of renal values. We are of the opinion that transplantation of the ureters into the bowel should rarely, if ever, be attempted, as the changes in the pelvis usually will make this operation difficult or impossible, and in many instances the renal damage is too marked to warrant the risk of further kidney infection from the intestinal tract. Ureterostomy, the transplantation of the ureters into the skin, may be resorted to but in many cases the upward spread of malignant disease, or extensive fibrosis will make the pelvic field unfavorable for this procedure. The most conservative program consistent with relief should be chosen for the patient with active carcinoma.

Ureteral dilatation is the simplest therapeutic measure. It is essentially palliative and has no lasting value where the blockage of the ureter is the result of tumor. We must dilate the ureters with great caution in such cases lest we precipitate complete occlusion and make surgical intervention imperative. Where the ureteral obstruction is due to fibrosis, dilatation is of great value.

It has been our experience that nephrostomy, either unilateral or bilateral, is the surgical procedure of choice to meet the conditions which arise from ureteral obstruction. It may be an emergency procedure or an operation of election. The results are frequently astounding and the operation can be performed without severe reaction on the part of the patient. It must be noted, however, that the results are better in the presence of definite obstructive pathology than in cases of non-obstructive pyelonephritis. In our previous communication on the subject, we enumerated the indications to be "the pain of ureteral and renal pelvis distention unrelieved by simpler measures, sepsis within the obstructed kidney, and the signs of advancing uremia with oliguria and anuria from extreme ureteral occlusion." We have employed bilateral nephrostomy in several instances with spectacular results.

The removal of a kidney is not often advisable in this group of individuals, especially in the presence of active malignant disease in the cervix. However, persistent pain, chills and fever, due to an active pyelonephritis in an obstructed kidney, might make nephrectomy justifiable. In the patient without active disease the removal of an infected functionless kidney is certainly warranted in the presence of a normal ureter and kidney on the other side. (Figs. 1 and 2.)

In this whole question of the treatment of the urinary complications of carcinoma of the cervix, one must be influenced by the entire urological picture, the extent and activity of the disease in the pelvis, the expectancy of life, and the general condition of the patient.

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COMMENTS ON THE TREATMENT OF THE RUPTURED URETHRA

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THE ultimate result which follows rupture of the male urethra is frequently most unsatisfactory. For the purpose of determining, if possible, the reasons for poor results I recently reviewed the records of patients with a history of old rupture of the urethra, who had been admitted to the Wisconsin General Hospital over a period of ten years. From this review the important reasons, I believe, fall into three general groups as follows:

1. *Failure of the Physician (and the Patient in Some Instances) to Recognize a Urethral Injury though Sufficient Objective and Subjective Symptoms Are Present to Definitely Establish the Existence of the Injury.* Obviously, this occurs only when the injury does not produce complete retention of urine. To illustrate this I relate the following instances:

A young man was crushed between two freight cars and the pelvis was fractured. Though there was hemorrhage from the urethra and blood in the urine, the attending surgeon centered his attention on the fracture of the pelvis. He not only failed to treat the urethra, but also failed to mention the injury to the patient. After complete healing of the fracture had occurred, but before the patient's claim against the railroad was settled, a very tight stricture of the urethra developed, which not only resulted in considerable suffering to the patient, but proved very expensive to the railroad company.

In 1933 a man of 42 was admitted to the hospital seventeen days after having been hit by a truck and knocked unconscious. Though he had hematuria for several days, he was permitted to continue work for seven days. During this time the attention of the attending physician was focused on a slight injury of the arm. About seven days after the injury a large swelling developed in the right inguinal region and in the upper thigh due to extravasation of urine. This was aspirated four times before the patient entered the hospital. A large quantity of urine was drawn off each time. Examination in the hospital revealed a rupture of the urethra and a satisfactory result followed a suprapubic cystostomy, drainage of the extravasated areas, and appropriate dilatation of the urethra.

2. *Inadequate or Inappropriate Treatment.* Often a suprapubic drainage is done soon after injury for the relief of complete retention resulting from a rupture of the urethra, but nothing is done to the urethra. Many weeks or even months later, when an effort is made to repair or to have repaired the urethra, the problem frequently taxes the ingenuity of the most skillful genito-urinary surgeon.

3. *Negligence of the Patient.* The failure of the patient to carry out over a period of years the treatment advised by the attending physician is commonly recognized as the source of much trouble.

It is well known that any portion of the urethra may be ruptured, though the most common locations for this injury are the bulbous and membranous areas. However, when seen soon after injury, certain principles of treatment apply to all of the severe injuries. These principles are:

1. *Constant, Adequate Drainage of the Urine.* This is essential. It is desirable to accomplish this away from the field of injury if possible. In doing so continued or repeated extravasations of urine are prevented. When the urine is not infected a

single extravasation usually does no harm, but if extravasation is permitted to continue over a period of time, and especially when catheterization has been attempted, infection will usually follow. On one occasion it was my misfortune to rupture the penile portion of the urethra while dilating a stricture. Great force was not used and the rupture was not suspected until the patient voided, when all of the urine extravasated into the tissues of the penis. A suprapubic cystostomy was performed immediately and the extravasated urine entirely absorbed within a period of twelve hours. Within ten days normal voiding occurred.

Healing of the damaged urethra progresses more satisfactorily when the urine is drained away from the field of injury. For drainage a suprapubic cystostomy should be done as soon after the injury as possible. A large soft rubber tube is placed well down to the base of the bladder. This probably gives the best drainage as it acts as a siphon and keeps the bladder entirely empty.

2. *The Urethral Channel Must Be Reestablished Soon after Injury.* The necessity for this can not be overemphasized. As a result of delay a relatively simple surgical problem becomes a very difficult one.

3. *The Caliber of the Urethra Should Be Maintained during the Healing Process.* This may be accomplished with the use of a soft rubber catheter, size 18 to 22 F. One end of the catheter is brought out through the suprapubic wound and the other through the meatus. It is not used for drainage of urine, but simply to maintain the caliber of the urethra and to iron out torn fragments of tissue, thereby preventing their healing in such a way as to lessen the caliber of the urethra. This tube should be left in place from 15 to 25 days. Some surgeons oppose this procedure, but in our experience it has proven satisfactory when the urine is kept out of the urethra. The same principle of treatment is used in the repair of the cut or torn ureter.

4. *The Caliber of the Urethra Must Be Permanently Maintained by Frequent Dilatations with Sounds.* During the first year sounds should be passed every few weeks (from two to six weeks). After the first year the interval is increased to from three to twelve months, but the procedure should never be entirely discontinued during the life time of the patient.

TREATMENT OF TYPES

Considerable latitude in the selection of treatment is permitted, the procedure to be followed depending upon the preference of the surgeon as well as upon the more important factors of the location and the extent of the injury. These wide variations are possible without sacrificing the basic principles of treatment outlined above. The procedures mentioned here are merely presented as those which have proved quite satisfactory in our hands.

Rupture of the Bulbous Urethra. This is the most common type of urethral rupture. It results from force applied to the perineum and is commonly referred to as "the straddle injury." It is characterized by hemorrhage from the meatus, hematuria and swelling in the perineum. To illustrate the type of procedure we frequently use in rupture of this part of the urethra, the following report of our most recent case is briefly mentioned.

J. P., age 44, while walking across a railroad trestle on May 1, 1937 fell astride a tie or rail and ruptured the bulbous urethra. He had hemorrhage from the meatus and retention of urine. A physician was unable to pass a catheter. Operation was performed on May 2, 1937. A suprapubic cystostomy was done and a filiform was successfully passed through the urethra from the bladder. By means of this a #22 F. soft rubber catheter was pulled into the urethra and left in place. The upper end was brought out through the suprapubic wound. A #30 F. catheter was introduced into the bladder for drainage. Though there was a small hematoma in the perineum it was not drained but was soon absorbed.

Convalescence was uneventful. The suprapubic catheter was removed on the 10th day and urethral catheter on the 18th day.

COMMENT

Perineal section is unnecessary when a catheter can be passed through both portions of the urethra, either from the meatus to the bladder or from the bladder to the meatus. If the hematoma (and extravasated urine) in the perineum is not extensive, and if infection does not occur, even though the urethra is completely severed, satisfactory healing will follow splinting of the urethra with a catheter without suturing the ends of the urethra.

The use of a urethral catheter alone as a means of drainage in those cases in which one can be passed is not, in my opinion, good practice except when the injury is very slight. It is true that many will recover satisfactorily with this treatment, but the complications which result from infection and extravasation will occur more often than when other means of drainage are used.

RUPTURE OF THE MEMBRANOUS URETHRA

This injury is usually seen in association with fracture of the pelvis. The urethra may simply be torn or it may be completely severed and the ends widely separated. The treatment indicated is perineal section with repair of the urethra over a catheter and a suprapubic cystostomy for drainage.

RUPTURE OF THE PENDULOUS PORTION OF THE URETHRA

Rupture of a severe degree in this part of the urethra occurs very infrequently. Minor tears occur most often from the passage of instruments. When a severe injury with extravasation is encountered suprapubic cystostomy should be done immediately. The penis should be elevated and hot applications should be applied. In two or three weeks the urethra should be gently dilated. This is repeated every two weeks for several times and then at less frequent intervals.

OLD INJURIES

These present multiple and serious problems. A number of ingenious operations have been devised for the correction of conditions resulting from these untreated or poorly treated cases. These conditions are so various that no general procedure can be described, and each case has to be treated as its peculiar complications demand.

THE TREATMENT OF HYPOSPADIAS

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THE basic requirements for a thoroughly satisfactory repair in hypospadias, as Cabot so clearly points out, are three-fold. It should effectually overcome the ventral curvature to produce a penis in which chordee does not occur, and with which satisfactory sexual intercourse can take place. It should overcome the disability of the absent urethra by supplying a new one through which a single urinary stream can be projected forwards with the patient standing. At the same time this urethra should be devoid of such new disabilities as stricture formation and the growth of hair within it. Finally, and most importantly, it should be sufficiently simple and certain of freedom from post-operative complications such as the formation of fistulae to enable it to be carried out with a reasonable prospect of success by a well trained surgeon.

One cannot emphasize too strongly the dual sexual and urinary function of the penis, and inasmuch as both of these functions are in abeyance in the hypospadiac, insist on the necessity for their complete and permanent restoration as the only criteria for a successful operation.

Perusal of the literature (well reviewed recently by Godard) describing the truly astonishing number of operations proposed for the condition, leaves one with the impression that the question of urethroplasty is far from solved, and that preoccupation with it has largely overshadowed the equally important question of penile efficiency. The fact that most surgeons who deal with the condition will admit to frequent, partial or complete failure, and that they constantly change their technique seeking new therapeutic light upon this difficult problem, supports this feeling. It is clear that most operations in vogue at present require the most delicate technical skill for their performance, and that success depends upon careful attention to the most minute details. The personal factor is great, and probably explains why certain authors report good results with a particular technique which is roundly condemned by others, who in turn as warmly advocate another method. It probably accounts for the melancholy experience of those surgeons who consider hypospadias to be inoperable. A notable feature of the literature is an absence of any careful evaluation of remote results, particularly in regard to the sexual aspect of the question. Very few of the proposed operations are free from objectionable features, and few indeed fulfil the ideals I have somewhat arbitrarily laid down.

Clinically, hypospadias presents itself as balanitic, penile, penoscrotal, scrotal and perineal. At the one end of the scale are those mild deficiencies of the terminal urethra which have little but an esthetic significance, and which it has been my practice to leave alone. At the other end are those vulviform types, which, with bilateral herniae and undescended testicles entail multiple operations for their cure, and so closely resemble the female genitalia as not infrequently to include a change of sex as part of the treatment. Between these two extremes come the majority of patients with penile, peno-scrotal and scrotal hypospadias, all of whom have from the practical standpoint two essential defects in common; namely, the dorsal preputial apron with unequal distribution of the dorsal and ventral penile skin, and a greater or lesser degree of approximation of the glans to the hypospadiac meatus due to the shortness of the urethral cord replacing the

absent portion of the urethra. It is common experience that, when the parts are carefully dissected free from the fibrous bands to establish this urethral defect to its widest limits and to make the penis and urethra occupy their normal relationships

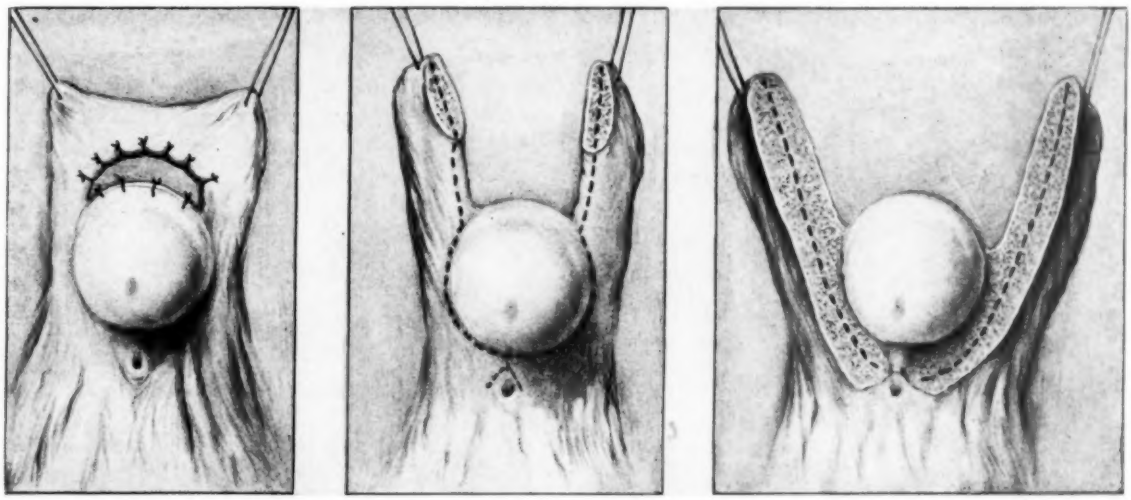

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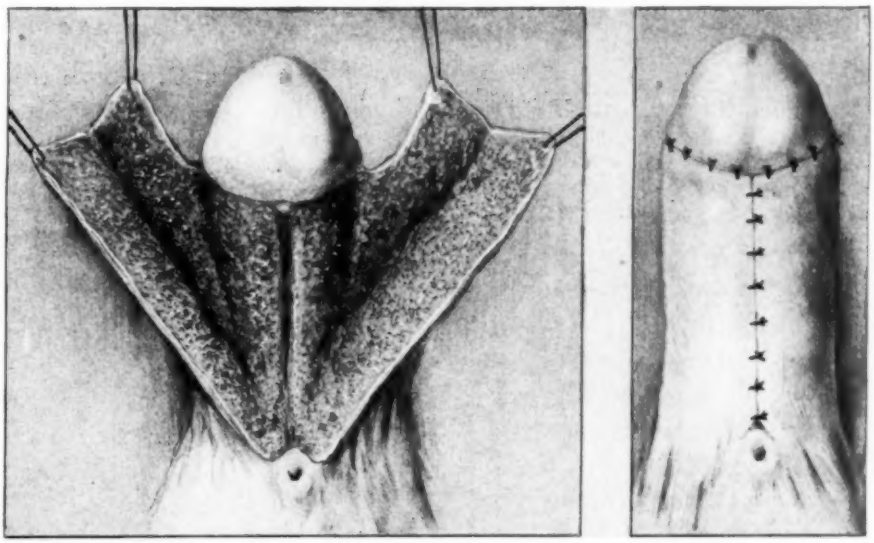
FIG. 1. Edmund's operation. (*a*) First stage. Buttonholing the preputial apron in order to increase the lateral blood supply. (*b*) and (*c*) Second stage. Performed three weeks later. The preputial pedicle is divided and each half opened out as indicated by the dotted lines.

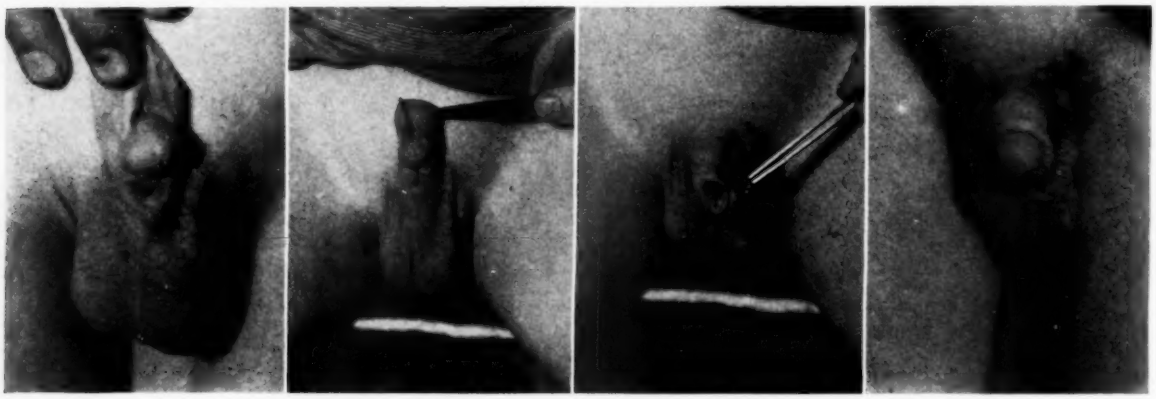


a *b*

FIG. 2. Edmund's operation. Second stage. (*a*) The two pedicles are converted into two lateral flaps. The corpora cavernosa exposed, and the urethral cord and all fibrous adhesions removed. The urethra is thrown back as far as it will go. (*b*) The two flaps are wrapped round the ventral penile surface and sutured as indicated. The final appearance should be that of a well circumcised penis.

which hold them together so that the penis can be fully extended and the urethra allowed to retreat posteriorly, a high proportion of the penile cases become peno-scrotal, the peno-scrotal become scrotal and the scrotal perineal. It is necessary before attempting to reconstruct the missing portion of the urethra. It is equally certain that this half of the problem should be attacked at an early age (two to three years) to enable normal development to proceed.

The problem of hypospadias falls thus into two parts. Firstly, the establishment of the complete urethral defect and the preputial apron in order to increase its blood supply so that all of this skin may safely be utilised in reconstructing the



a *b* *c* *d*

Fig. 3. (*a*) Scrotal hypospadias in a patient in whom two wholly unsuccessful operations had been performed. The preputial apron had never been utilised in any way when straightening was attempted. (*b*) The preputial apron buttonholed. (*c*) The pedicled prepuce turned down to show how the glans could be passed through the hole. (*d*) The result of incorporating the pedicled flaps in the ventral surface and removing the ventral adhesions. The appearance is that of a well circumcised penis. The urethra has now been constructed.

redistribution of the penile skin. Upon the successful performance of this depends the sexual future of the patient. Secondly, the construction of a new urethra which will render the patient potent and able to micturate efficiently.

ESTABLISHMENT OF THE COMPLETE URETHRAL DEFECT AND REDISTRIBUTION OF THE PENILE SKIN

The importance of this step cannot be fully realised by those who are satisfied with the effects of ventral transverse incisions, for such a method cannot possibly cure what is, after all, a very complicated defect and one which lends itself extraordinarily well to the application of correct plastic principles. I am sure that no operation has been devised which equals that proposed by Edmunds, and as its principles appear to be little understood I shall deal with it fully. The criticism has been levelled at this operation that it requires special technical ability and dressmaking knowledge to accomplish it (Browne), but this is not so. Three steps, performed in two operations, are essential: firstly, a tube pedicle is prepared from the ventral skin loss; secondly, the urethral cord and the remains of the corpus spongiosum must be completely removed without damage to the corpora cavernosa, and at the same time the hypospadiac meatus and urethra must be thrown back to that point in the penis, scrotum or perineum where they occupy their normal position; thirdly, the tubed dorsal prepuce must be unfolded and the flaps so formed incorporated into the ventral length. The result of these operations should be over-correction of the ventral curvature and thorough establishment of the real as against the apparent urethral defect.

TECHNIQUE

Operation I. (Fig. 1*a*.) With two tiny holding sutures the preputial apron is elevated from the glans and held out flat. A buttonhole is then made just beyond the level of the corona through both layers of skin so that the glans can be conveniently pushed through it from the ventral to the dorsal aspect. The edges of the buttonhole are then sewn round with fine interrupted silk upon an eyeless needle. The preputial apron is thus converted into a tubed pedicle

based on lateral roots, and is left for three weeks to a month before proceeding with Operation II.

Operation II. (Fig. 1*b* and *c*.) The tubed pedicle is now divided transversely at its mid-point so that each half is left attached to the lateral aspect of the glans. A longitudinal incision is now made from the hypospadiac meatus, ventrally along the penis to the point where the frenum is normally attached. It is then carried out laterally round the inferior surface of the glans on either side, just below the level of the corona, and continued along the lateral pedicles to their ends, where the buttonhole suture line lies. Each tiny tubed pedicle is then laid completely open and the penile skin on either side dissected extensively away from the corpora cavernosa. (Fig. 2*a*.) The urethral defect is thus exposed and the fibrous tissue representing the remains of the urethra and corpus spongiosum dissected away from the corpora cavernosa without damage to them. At the same time the urethra is undermined and released from any fibrous adhesions which hold it forward, so allowing it to slide back along the shaft of the penis as far as it is possible to make it go. If this step is efficiently carried out it will be found that the hypospadiac meatus retreats in the penile cases into the scrotum, and in the penoscrotal cases into the perineum. After all hemorrhage has been arrested, the two flaps on either side are then sutured in the midline as indicated in the diagram (Fig. 2*b*), so bringing the dorsal excess on to the ventral surface and increasing very markedly the ventral length from the frenum to the hypospadiac opening. Quarter-inch gauze tape is wound round the penis and soaked in mastisol so that when it sets, a little case is produced which exerts firm pressure on the flaps. A catheter is left in the bladder for twenty-four hours to prevent urine coming in contact with the suture line until it is sealed. Sutures are removed in six or seven days. (Fig. 3.) No further operations are undertaken until the child is 7 or 8 years of age, when the development of the parts will warrant urethral reconstruction.

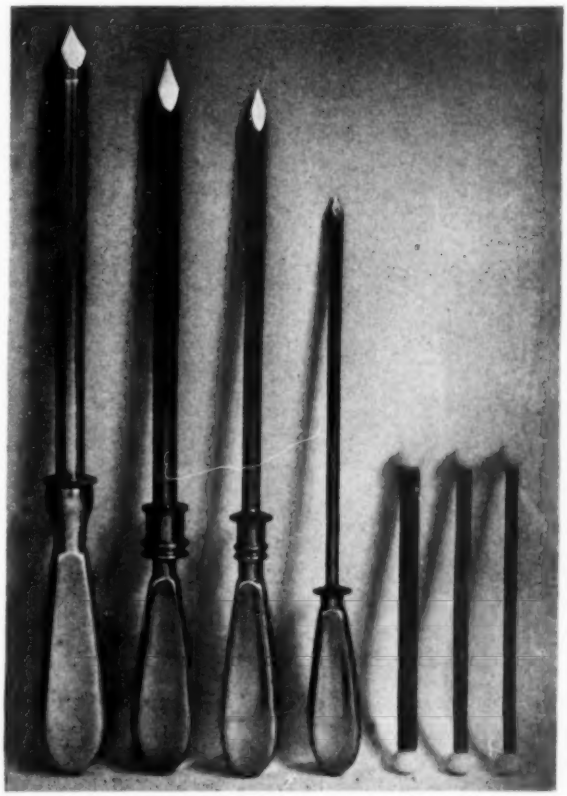


Fig. 4. The author's skin graft introducers and dilators. The former will carry in the barrel thin skin covered catheters from 5E to 11E. The dilators are of gum elastic and have "screw-on" ivory ends so that they will not slip out. When reinserting them a small olive point is substituted for the ivory end.

THE URETHRAL RECONSTRUCTION

Of the innumerable operations proposed for the reconstruction of the absent urethra, all of them rely upon one of three different methods of plastic repair; namely, the use of local flaps, tubed pedicles, or free grafts. The first is represented by the various modifications of the Marion Duplay or Thiersch Duplay procedure, Bucknall's operation with its modifications, and Ombredanne's operation. The second depends upon the use of extraneous tissue transplanted from a distance by means of the Gillies tubed pedicle. Free grafts are made use of in the procedures of Nové Josserand, Rochet and Mayo. Briefly, flap

operations are most widely practised and are in vogue throughout the world, tubed pedicles are utilised only by those who have had special experience with them, while free grafts have been generally condemned and have fallen into disuse.

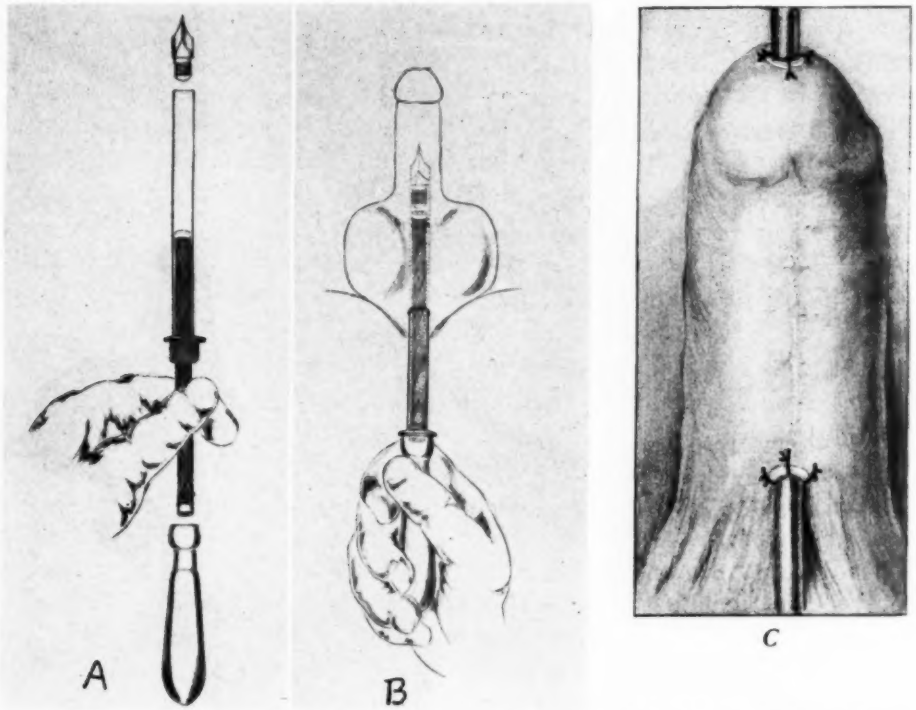


FIG. 5. (A, B, and C) Method of loading the introducer with skin covered catheter and passing it from the perineum along the shaft of the penis. After withdrawal of the barrel, the graft lies as in (C).

My own fairly extensive experience with flap operations and tube pedicle grafts in their innumerable modifications is that they are difficult to perform, requiring special technique, are liable to heartbreaking partial or complete failure of union with resultant formation of fistulae during the post-operative course: finally, all too high a percentage develop intra-urethral hairs in later life. It is unfortunate that this last complication is now more commonly reported in Ombredanne's operation—hitherto regarded as probably the most satisfactory and foolproof of all the flap methods. A more valid objection to their use, however, is that they are technically beyond the scope of the general surgeon.

When one turns to the literature on the use of free grafts, one can only be depressed by the dismal record of failure which seems to have resulted from this method, but to anyone with experience of the great success of the Esser principle of inlay grafting in its modern form, this would appear to be the most reasonable method of constructing a new hairless urethra with a high degree of certainty, without utilising penile skin, and with none of the dangers of breaking down association with suture lines in this region.

PRINCIPLES OF THE OPERATION

Nové-Josserand proposed that after the usual straightening of the ventral curvature, a tunnel should be bored through the penis from the posterior fistula to the tip of the glans and a catheter covered with Thiersch graft be inserted into the canal. He recommended that the catheter should be removed at the end of eight to ten days and the skin-lined passage be dilated periodically with bougies. Anyone with an intimate knowledge of the behaviour of the grafted skin will admit the immediate criticisms that such contraction occurs—

that the canal becomes hopelessly stenosed and periodic dilatation fails to maintain its patency. This is, in fact, the uniform result of the operation, and explains why it has fallen into disuse.

The modern epithelial inlay demands the introduction of thin, hairless epidermis into a subcutaneous cavity, made larger than the ultimate size required, and maintained in a distended position for a period which exceeds by a considerable margin the contractile phase of grafted skin; namely, about six months. Under these conditions an epithelial canal can be constructed in which stenosis does not occur.

I was first encouraged to try the effect of a penile epithelial inlay in an adult patient with hypospadias in whom so many operations of a flap type had been performed that the ventral skin of the penis was scarred beyond any hope of making local flaps. After constructing a tunnel through the penis, I introduced a skin-covered catheter and maintained the patency of the new canal continuously for a period of six months. At the end of that time, the

Fig. 6A. Vulviform hypospadias, in which the sex of the patient was for some time in question. Bilateral hernia and undescended testicles.

Fig. 6B. Shows the marked ventral fixation of the glans, the perineal meatus and the dorsal prepuce.

Fig. 6C. After bilateral herniotomy, Meyer Torek operations for undescended testes, and Edmund's operation to straighten the penis. This was done at one sitting.

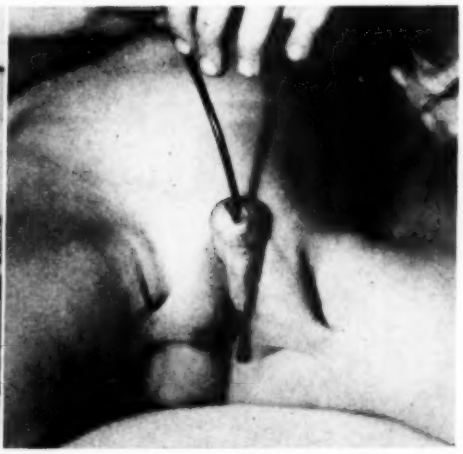


Fig. 6D. After the inlay operation for urethral construction. The urethra is soft and supple and a 7E catheter passes easily. Anastomosis has not yet been made, nor the scrotum united. This will be done in six months' time.

proximal end of the new canal was anastomosed to the hypospadiac meatus with such a satisfactory result that I have employed the same principle on other cases with gratifying results. Since then the method has been extended to children with equally satisfactory results, and on the whole I believe it to be well within the capabilities of any well trained surgeon.

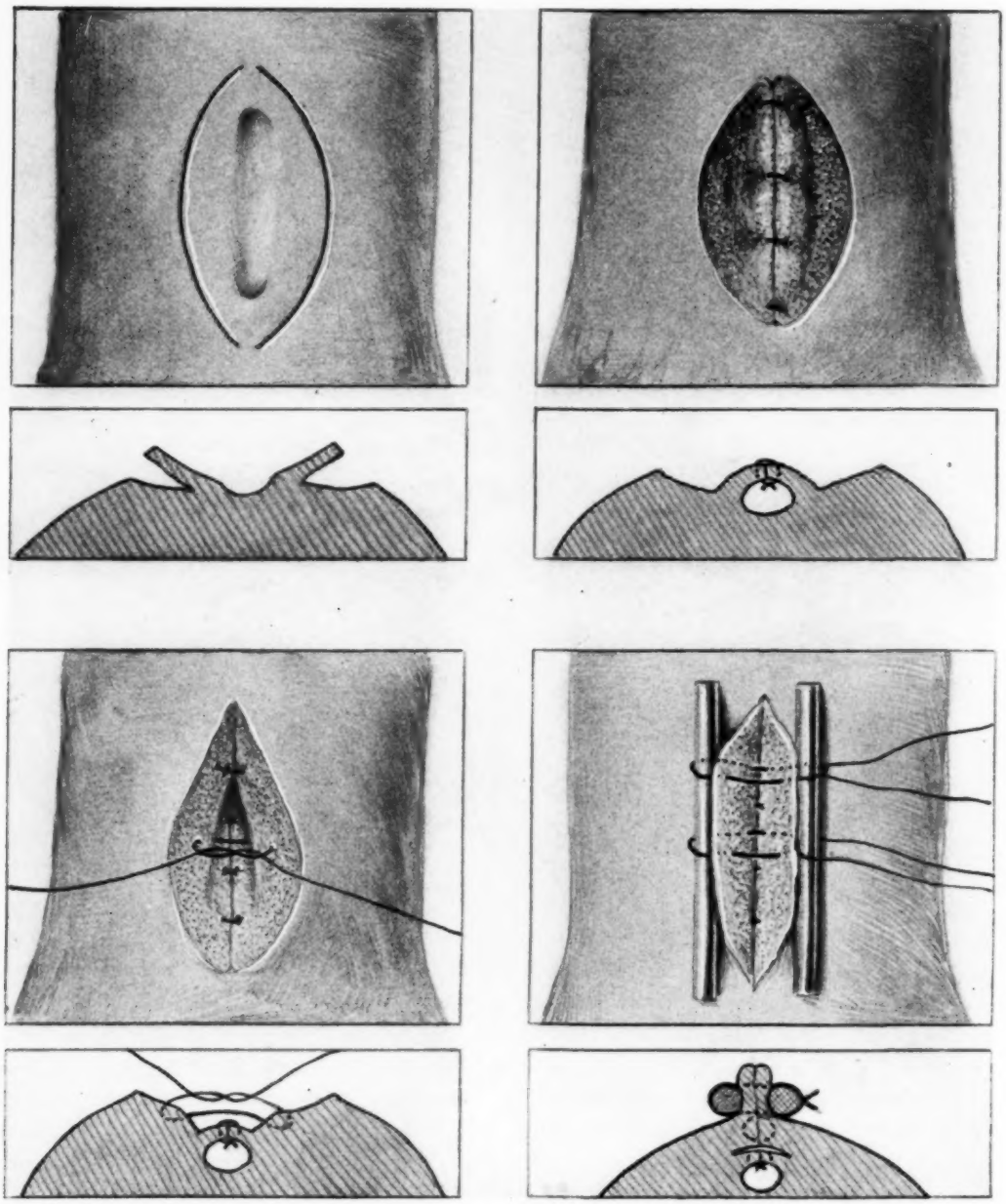


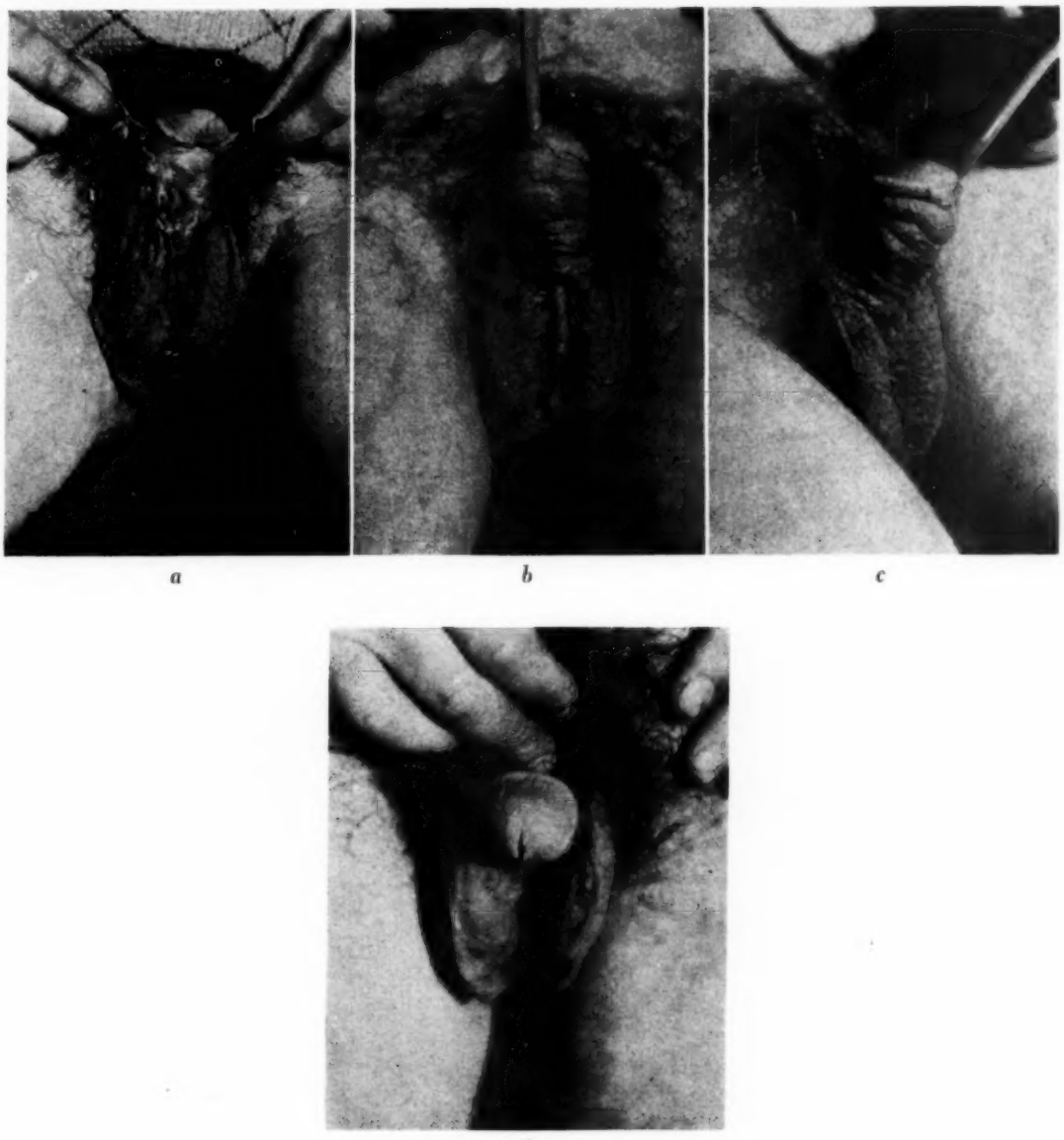
Fig. 7. End-to-end anastomosis of the new urethra and the hypospadiac meatus.

The method, however, has been considerably modified. It would seem a comparatively simple matter to introduce a skin-covered catheter through the penile tunnel. It is, in fact, extraordinarily difficult to do so, and at the same time to prevent the graft being rucked off the catheter during its passage along the tunnel. An introducer was therefore devised which overcomes this difficulty and renders the operation extremely easy. This I have made in several sizes, according to the development of the patient. (Fig. 4.) The

instrument resembles a large suprapubic trocar, except that the handle and the cutting point can be unscrewed, leaving a smooth hollow barrel 5 inches long, with an internal diameter sufficient to admit a gum-elastic catheter of appropriate size covered with Thiersch graft.

TECHNIQUE OF THE OPERATION

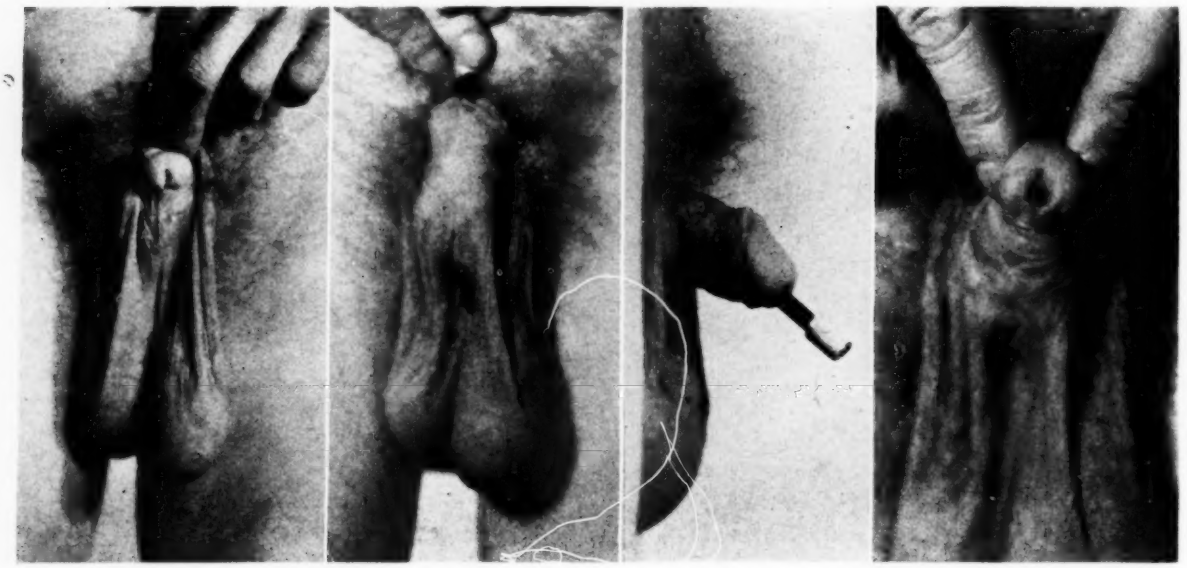
The operation is performed, after the usual readjustment of the dorsal prepuce and the straightening of the ventral curvature, about the seventh to ninth year. A thin razor graft, or Thiersch graft, is cut from the inner side of the arm and carefully



a *b* *c* *d*

FIG. 8. (*a*) Scrotal hypospadias after seven unsuccessful operations. (*b*) After Edmund's operation and the author's inlay method of constructing the urethra. No. 10E catheter passes easily. (*c*) Six months after end-to-end anastomosis, showing the complete correction of the ventral curve and the total absence of stenosis. The patient has now had for two years a penis with perfect urinary and sexual function. (*d*) Recent photograph of patient shown in 8*a*, *b*, *c*. The meatus is slit-like and of entirely normal appearance. The urethra is soft, elastic, and is developing a certain degree of normal distensibility.

applied, raw surface outwards, like a cigarette paper, to a piece of gum-elastic catheter, which just fits in width and undisturbed. (Fig. 5*c*.) One-inch gauze tape soaked in mastisol is then bandaged round the penis fairly firmly so that when the



a *b* *c* *d*

Fig. 9. (*a*) Primary adult scrotal hypospadias. Marked fixation of the glans. (*b*) After Edmund's operation and author's urethral inlay. (*c*) Lateral view to show correction of ventral curve. (*d*) Anastomosis performed. Note the normal appearance of the meatus. The patient not only micturates perfectly, but is sexually efficient.

length the barrel of the trocar. The graft is tied at either end with a single strand of 000000 catgut. It is then carefully placed in the barrel of the instrument and the cutting point and handle are screwed into position. (Fig. 5*a*.)

With the patient in the lithotomy position, a small stab incision is made just distally to the perineal meatus and another at the dimple usually present at the tip of the glans. The trocar introducer is then thrust subcutaneously along the penis from the posterior stab incision until the point emerges at the tip of the penis. (Fig. 5*b*.) The maneuver, while not easy, can be facilitated by introducing a long slender pair of scissors with Mayo points in order to divide any fibrous bands which may obstruct the onward passage of the instrument. When it emerges, the cutting point of the introducer is unscrewed and the end of the skin-covered catheter is gripped firmly with a pair of forceps. The barrel of the instrument is carefully withdrawn through the posterior opening, leaving the catheter in place and its skin covering mastisol sets, an efficient casing results which maintains the necessary pressure on the graft and prevents erection of the organ. The entire procedure need not take more than twenty minutes to perform. It is advisable to place a catheter in the bladder for forty-eight hours, through the hypospadiac meatus, in order to prevent urine coming in contact with the graft.

At the end of ten days the case is removed, the catheter withdrawn, and the skin-lined urethra is syringed through with saline solution or half-strength eusol. A permanent dilator of suitable size is then introduced into the urethra, and at no time for the next three to six months is this left out for more than the five or ten minutes required to cleanse the canal. (Fig. 6.) It is necessary to make this point absolutely clear to the patient and the parents, for twenty-four hours without the catheter will cause hopeless stenosis of the cavity during the early stages. These dilators are again of various sizes with screw on ends to prevent their slipping out. (Fig. 4.) They act, in fact, like the gold

"sleepers" which all jewellers have used from time immemorial after piercing the ears.

After six months the contractile phase should be over, and the dilator can be safely left out. Anastomosis of the posterior end of the new urethra and the hypospadiac fistula is then performed over a short piece of catheter. (Figs. 7, 8, 9.) The nearer the perineum this anastomosis can be made, the easier it is to perform. If possible, anastomosis is avoided at the peno-scrotal angle, a point where an end-to-end union can be troublesome. Care is taken to see that the knots suturing the tiny lining flaps are drawn into the urethral canal. If there is any difficulty about this, Edmunds' method of passing a threaded needle backwards along the urethra in order to catch the knots and draw them through is useful. The external covering flaps are sutured with "end-on" mattress sutures of ophthalmic silkworm-gut, or fine silk on eyeless needles. Quilting is advantageous.

ADVANTAGES AND DIFFICULTIES

The advantages of this operation are many. It does not require the diversion of the urinary stream at any time during its performance, and a short piece of catheter is really only required at the last stage of end-to-end anastomosis. I am not sure whether even then it is really necessary. The introduction of the skin-covered catheter is rendered easy by means of the introducer, and this important stage need take only a few minutes.

As with other types of inlay graft, a perfect take should result in a very high percentage of cases, while continuous dilatation maintained until the contractile phase of the grafted skin is well over, prevents subsequent shrinking and stenosis. The appearance from the cosmetic stand-point is much superior to that of any other method, particularly at the meatus, which is placed at its correct anatomical position at the tip of the glans. Thus the urinary stream is likely to be better projected than following operations of the flap type, where the meatus is more ventrally situated and a certain amount of spraying is common. Another important advantage is that hair need not be included in the urethral lining—an all too common result of the flap operation.

The total time taken to make a functioning urethra is, I think, rather longer than with other methods, owing to the prolonged period of continuous dilatation necessary, somewhere about nine to twelve months elapsing from start to finish. On the other hand, the actual period of hospitalisation is relatively short—five to six weeks—while between operations the patient is perfectly able to conduct a normal life. From the surgical point of view, one is freed from the tiresome and irritating business of closing and reclosing the fistulae which so often develop in adult patients along the suture line of the flap operation.

The difficulties of the operation are chiefly concerned, first, with cutting a perfect Thiersch graft, and secondly, performing with considerable refinement of technique an end-to-end anastomosis of the new urethra to the hypospadiac meatus. The first requires a certain amount of practice; the latter is made easier because it can be done at a point in the perineum or scrotum where a substantial mass of tissue can be brought in from the sides to reinforce the internal suture line and so largely diminish the chance of leakage.

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HORMONAL AND SURGICAL BASES FOR TREATMENT OF UNDESCENDED TESTIS*

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DURING the past three or four years the treatment of the undescended testis has been monopolized by the exponents of hormonal therapy. Surgery has been relegated to the sidelines. The magic hormone has cured as high as 100 per cent of cases in some clinics. Surgery, on the other hand, has never claimed success in every case by a single operative procedure. Since the surgeon realizes that it is extremely difficult to transplant the testicle in some cases of cryptorchidism, he may rightly criticize the hormonal adherents for claiming such a high percentage of cures. There is no doubt that a certain percentage of cryptorchids responds to hormonal treatment. The same group of patients may not be difficult to treat with surgery. May not some be spared a surgical procedure and should not others be spared needless hormonal treatment? Is it not possible that the patient may be benefited by the application of both forms of treatment where either one alone fails? It is time that we evaluate the factors involved in these two methods and correlate the scientific data to form a basis for the present day treatment.

There is a cause for every undescended testis. The surgeon has the advantage in studying the actual factors which prevent the descent of the testis, while the hormonal therapist can only hypothesize or, perhaps, credit the abnormality to "intersexuality." There are a moderate number of cryptorchids in whom the descent of the testis is checked by slight adhesions, by hernia or malformations or by mal-insertion of the gubernaculum. In other cases the testes remain intra-abdominal with a mesentery or have short vessels and vasa. The testes may be retained as a result of strong inflammatory adhesions or ectopy. By ascertaining the causes of the undescended testis, the action of the gonadotropic factor and the efficacy of surgical procedures, one is able to reconstruct a rational form of treatment.

In order that we may determine the principles governing the choice of a method of treatment, whether the administration of the gonadotropic factor or the application of surgery, it is first necessary that we comprehend as fully as possible the action of the gonadotropic principle. Halban has shown that the newborn have swelling and edema of the external genitalia due to excessive amounts of the hormone which can be demonstrated in the blood and urine of the infant for the first four or five days. Engle, Moore, and Aberle and Jenkins, in applying the gonadotropic principle to the pre-adolescent macaque monkey, have produced a descent of the testis with an associated edema of the genitalia similar to that seen in the human newborn. Since the same hormone is present under both conditions, it is safe to assume from the work of Schapiro, and Goldman and Stern, and Aberle and Jenkins that the same processes are activated. The interstitial tissue of the testis is increased and the cord structures are elongated.

In order to enlarge our knowledge of what actually takes place in the inguinal canal and scrotum during the period of testicular descent it has been necessary to study these structures in greater detail before and after the administration of the gonadotropic principle in the pre-

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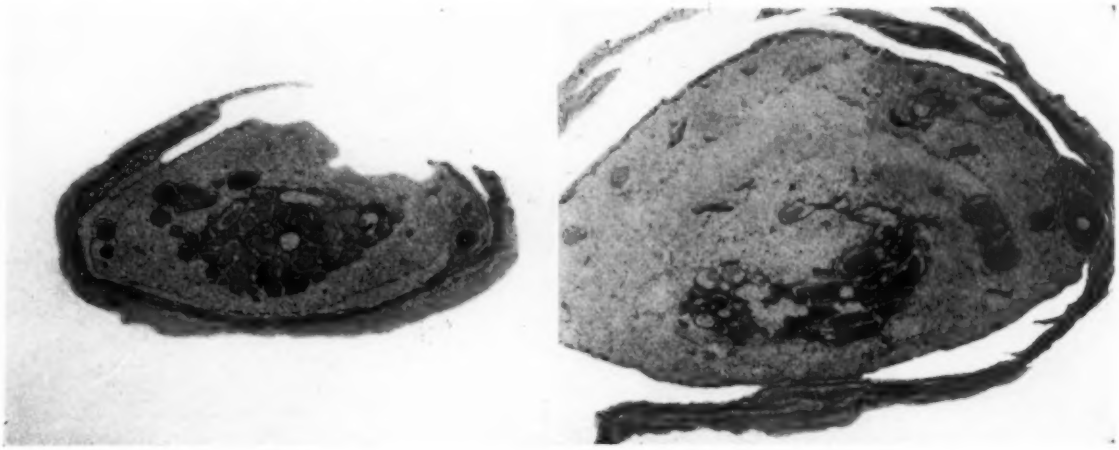
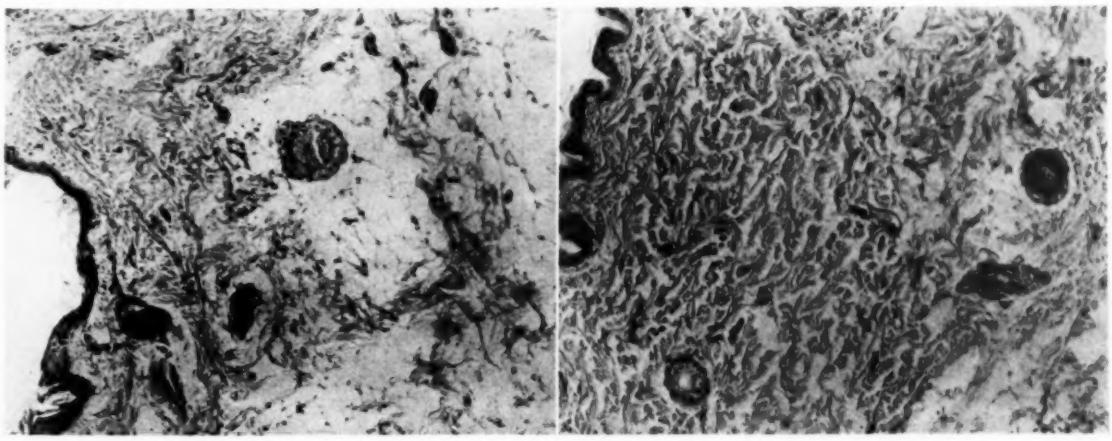
adolescent macaque monkey. The right inguinal canal and its contents and the testis were excised prior to treatment. enlarged two or three times. The scrotum showed a greatly thickened wall, a hyperplasia of the dartos muscle and an increased



A B

Fig. 1A. Photomicrograph (× 8) of right inguinal canal of monkey, before treatment with the hormone. B, photomicrograph (× 8) of left inguinal canal of monkey, after complete descent of the testis with four weeks of gonadotropic treatment. Note the great increase in size of cord, deposit of fatty tissue, enlargement of the vessels, and change in size of vas and cremaster muscle.

The gonadotropic factor was administered in an amount sufficient to produce a descent of the left testis, after which the left inguinal canal and contents and the vascularity and thickening of the loose areolar tissue without any histological change in the skin (Fig. 2). The left vas was enlarged to three times the size of the



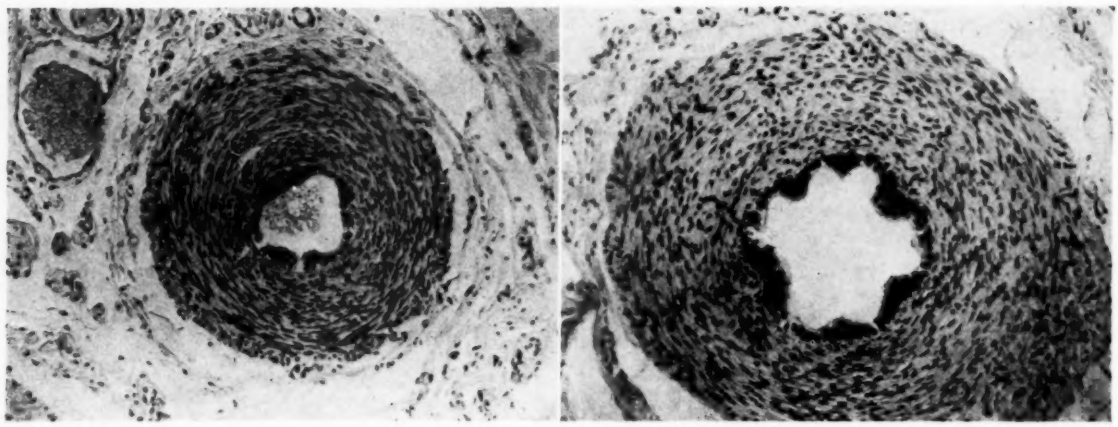
A B

Fig. 2A. Photomicrograph (× 65) of right scrotum of monkey, before treatment with the hormone. B, photomicrograph (× 65) of left scrotum of monkey, after complete descent of the testis with four weeks of gonadotropic treatment. Note the hyperplasia and hypertrophy of the dartos muscle, increased vascularity but no change in the skin layers.

testicle were removed for histological study (Fig. 1B). The left inguinal canal was found to be about three times as large as the canal on the right side (Fig. 1A). It was more vascular and there had been an increase in the deposit of fat. The cremaster was right vas due to the increase in its musculature, especially the circular and outer longitudinal fibers (Fig. 3). The vessels of the cord had also increased in caliber and in thickness of their walls (Fig. 4). The testis was enlarged and had become more

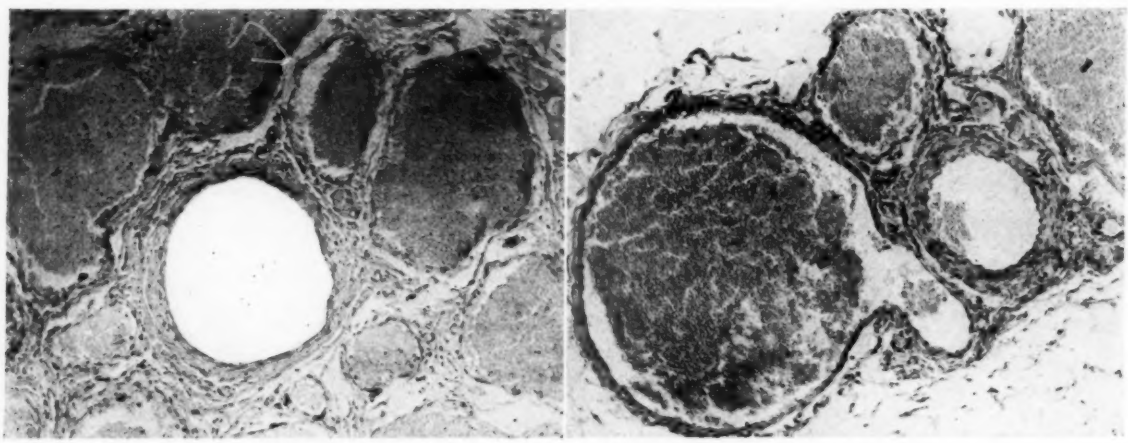
movable but there was no evidence of gametogenetic activity.

We thus recognize the results of the action of the hormone on the local tissues of the cord and the canal, but we remain ignorant of the manner in which the forces actually work to produce descent. Many writers have claimed that the gubernaculum pulls the testis into the scrotum. Hunter, Brugnone, Curling and Follin admit that the gubernaculum contains muscle fibers but believe that it does not cause a descent of the testis. Burdach has shown that the descent of the testis in a normal child is accomplished long before the muscle fibers of the gubernaculum can be demonstrated. Haller attempted to explain the descent of the testis by its increased weight. However, it is the consensus of opinion today that the gubernaculum is a guide or a rudder and not a tractor for the testis.



A B

Fig. 3A. Photomicrograph (× 85) of right vas of monkey, before treatment with the hormone. B, photomicrograph of left vas of monkey after complete descent of the testis with four weeks of gonadotropic treatment. Note the increase in size of the vas, especially the outer longitudinal and circular muscular fibers, increase in lumen and heaping up of the epithelium.



A B

Fig. 4A. Photomicrograph (× 65) of vessels of right cord of monkey, before treatment with the hormone. B, photomicrograph (× 65) of vessels of left cord of monkey, after descent of testis with four weeks treatment with gonadotropic factor. Note the increase in size of the muscular wall of both arteries and veins.

The function of the cremaster muscle in producing descent of the testis is not fully understood. The cremaster is innervated by a branch of the genitocrural nerve and is, therefore, a genital muscle. It is derived from the internal oblique muscle,

surrounds the cord and is inserted in the tunica vaginalis and the spine of the pubis. Hart demonstrated in the rat kangaroo that the cremaster grows upward and is attached to the inguinal bursa of the peritoneum in which the undescended testis lies. As the inguinal canal grows it enlarges upward and envelops the testis. He likens the condition to that of the urinary bladder, which in embryological development is intra-abdominal and which later becomes intrapelvic by the upward growth of the pelvic cavity. Undoubtedly the cremaster plays a part in the elevation of the testicle in man and animal. Does it play a part in its descent?

The sum total of the knowledge of the action of the gonadotropic factor is that it enlarges the inguinal canal, increases the size and weight of the testis, elongates the cord and prepares the scrotum for the reception of the testis.

The exact time for the application of this treatment is considered to be before the fifth year. Some writers prefer to give it earlier. Cooper claims to have found anatomical defects in the undescended testes of boys over two and one-half or three years of age in a large series of cases. He states that there was a reduction in the number and size of the tubules and an increase in the intervening stroma. The higher in the inguinal canal was the organ the greater were its defects. Drake, in analyzing a series of cases of undescended testes in boys from nine to nineteen years of age, found that in 23 of 35 persons full descent of the testes occurred during puberty. It is the general opinion that the undescended testis in the adult is aspermatogenic in about 65 per cent of cases and that those testes which are spermatogenic maintain such a function for a short time only. The weight of the evidence, therefore, is in favor of early application of the gonadotropic therapy, preferably between the second and third years.

The gonadotropic treatment can be readily applied at this age. Intramuscular injections of 0.4 to 1 c.c. of a solution which has the equivalent of 100 rat units to the cubic centimeter are given on alternate days for a period of one month. If the testis does not descend, the treatment should be repeated in two months. In the majority of cases, testes which respond to this treatment do so during the first series of injections, and if the second series is unsuccessful further hormonal treatment will probably be ineffective. Approximately 45 to 50 per cent of undescended testes can be made to occupy the scrotum by this method. Descent of the testes in individuals past puberty can not be expected by hormonal therapy.

The author has never seen any unfavorable reaction or harm resulting from this treatment. The gonadotropic factor does not produce gametogenetic maturity. Cabot states that the use of the gonadotropic principle may be dangerous in adults and he cites 3 cases in which death followed apparent allergic shock. It is, therefore, well to give a word of warning.

The surgeon is able to place the undescended testis in the scrotum without difficulty if the ectopic organ has come through the external ring and is lying on the anterior abdominal wall. Furthermore, testes which lie in the canal usually have sufficient length of vas and vessels to allow the testis to be placed in the scrotum. Barring rare accidents when the blood supply is destroyed by rough surgeons, these cases offer no particular difficulty.

Certain outstanding difficulties are encountered in surgical procedures when the scrotum is undeveloped, when the testis is malformed and small or associated with a large hernia, or when the testis with short vessels and vas is situated intra-abdominally. Bevan has contributed more than anyone to the surgical solution of the last problem by advising minute and careful dissection and division of all adhesions, which are numerous between the vessels and the vas. He obtains greater length by ligating the vessels to the testis and relies on the blood supply of the vas to give sufficient blood supply to the transplanted

testis. In the hands of many surgeons this procedure has resulted in an atrophy of the organ with a complete loss of its function.

Few surgeons have realized that in order to obtain length of the cord the testis and its cord structures may be brought under the inferior epigastric artery or that a similar result may be secured by the division of this artery. In this procedure the testis should be brought up directly behind the pubis and out through the external ring. The inguinal canal is closed firmly by plicating the muscles. An increase of 3 or 4 cm. in the length of the cord is obtained by this method. Torek has recognized the advantage of holding the testis in the scrotum until the scrotum is entirely developed and ready to retain the organ. The principle is excellent.

While the adaptation of the treatment depends upon the individual case, the members of both schools of treatment are able to produce descent of the testis and elongation of the cord by their respective methods in a certain percentage of cases. The hormonal therapist is able to elongate the cord structures and to enlarge the inguinal canal by stimulating the natural processes of development. The surgeon mechanically enlarges the canal and frees the adhesions along the intra-cord structures to give length and to allow deposition of the testis in the scrotum.

There is a group of cases in which either treatment alone fails: cases in which the testis is intra-abdominal, has a short vas and vessels or is malformed. For this group, successful results may be obtained by the use of both forms of treatment. If the surgeon will take advantage of the hormonal action prior to operative treatment, the difficult transplantations will be made easy and the probability is greater of the testis' retaining its place in the scrotum rather than of later retracting to the pubic spine or into the inguinal canal. When a case has not been treated prior to operation and the transplantation of the testis into the scrotum has placed the vas and vessels under a high degree of tension, the surgeon may immediately supplement the surgical procedure with a course of hormonal therapy. The increase in the vascularity of the cord and testis is accelerated and if the testis is smaller than its fellow it readily becomes of equal size. The scrotum develops more rapidly than it does by the simple presence of the testis. The author has followed this method in several cases with excellent results.

SUMMARY

The status of the hormonal and surgical methods of treatment for the undescended testis depends upon our present knowledge of the action of the gonadotropic factor and the limits of effectual surgery. Each method is well adapted to about 50 per cent of cases. Hormonal therapy will prevent a number of operative procedures. On the contrary, surgical treatment is necessary for a certain group. Another group of cases is best treated by a combination of the hormonal and surgical methods. Those patients whose testes are situated high will respond better to surgical treatment if they are given preoperative treatment with the gonadotropic hormone. Other cases which would be partial or complete surgical failures are made successful by the postoperative administration of the gonadotropic factor which relieves the tension on the cord and prevents retraction of the testis.

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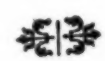

Hematuria is the most characteristic symptom of renal injury. In a few cases it is not present or its presence is not discovered early because of the inhibition of renal function that sometimes accompanies the injury. From—"Modern Urology" Edited by Hugh Cabot, M.D., C.M.G., F.A.C.S.

TOTAL CYSTECTOMY FOR INFILTRATING CARCINOMA OF THE BLADDER

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NEW YORK CITY

DURING recent years, considerable interest has been shown by surgeons in the possibility of curing certain types of carcinoma of the bladder by total cystectomy.[1] In various clinics in the last two decades, several series of total cystectomy cases have been published, and varying techniques have been used to remove the bladder, as well as to deflect the urine from the kidneys.

The ideal procedure in connection with total removal of the bladder would be a deflection of the urine through the ureters into the sigmoid and, at the same operation, removal of the bladder with adjacent glands, plus the upper half of the prostate. In view of the mortality attending such a procedure, it has not been feasible to introduce this as a routine operation, and most surgeons have been forced to accommodate themselves to a less ideal procedure, either dividing the operation into stages, transplanting one or both ureters (simultaneously) into the sigmoid, and at a later stage doing a cystectomy;[2] or doing a one stage operation, i.e. ureter implantations into the skin and total cystectomy at the same time. This latter procedure is the operation of election in my clinic, and even though it may not produce an ideal condition for the patient, most of the patients who survived the operation are comfortable and can readily be kept clean without any leakage along the drainage tubes, which are inserted through the ureter ostia into the kidney pelves.

Several moderately complete analyses of the mortality following ureterosigmoid implantations preliminary to total cystectomy in patients suffering from cancer of the bladder have been made. Naturally, the many cases that died as the result of the ureteral anastomosis and therefore never reached the stage of the cystectomy, are rarely recorded in the literature. If these cases could be assembled, I fear the mortality data collected by Papin and Hinman would show an enormous increase over the 50.7 per cent to 59.2 per cent which they have estimated[3] (based on some 203 and 181 cases published in the literature of this subject) as the present death rate of primary uretero-sigmoid anastomoses, followed by total cystectomy for cancer. Perhaps with simpler surgical technique, with the use of fewer sutures and more reliance on the sigmoid peritoneum to fix the ureter in its submucous trough, these results will improve and approximate the more satisfactory results obtained in non-malignant cases. Owing to the fact that frequently these ureters in cancer cases are thickened, dilated and infected, the problem is rendered more difficult.

In view of these data, it seems preferable to use the technique of skin implantation of the ureters with its lower operative mortality than the more ideal technique of ureter implantation into the sigmoid, followed by a second or third stage operation of total cystectomy. An analogous problem presents itself to the surgeon in attempts to cure recto-sigmoid carcinoma.

[1] v. Coffey, Lower, Quinby, Wade, Fedoroff, Smith, Nesbitt, Hinman, Higgins, Hryntshak, Heitz-Boyer, Scheele, Pleschner, Fey, Ward.

[2] Quinby transplants one ureter into the sigmoid and later transplants the second ureter at the same time that he performs the cystectomy.

[3] BEER, E. Technical Supplement of the Urologic and Cutaneous Review, III: No. 4, 279–283, 1915; *Ann. Surg.*, 90: 864–866 (November) 1929; Tumors of the Urinary Bladder. Baltimore, William Wood & Co. 1935, p. 104.

The best results in these cases are undoubtedly obtained by removal of the lower sigmoid and rectum, and establishment of a sigmoid iliac anus. This operation, known as the Miles-Quenu, gives the patients a fair chance of cure, though it does, of necessity, compel the patient to carry an artificial anus. Similarly in the technique of total cystectomy in one step with ureter implantation into the skin, the patients are incommoded to the extent that they must carry tubes in the ureters, which collect urine and pass it on to a urinal, but judging from cases which I have seen, this is not a serious inconvenience, and much less objectionable than an artificial anus in the sigmoid.

No matter what disposition of the ureters is made, there is always the complication of recurrent attacks of pyelonephritis and stone formation. With the ureters in the skin, irrigations of the upper tract can be carried out and small calculi or phosphatic incrustations can be washed out, whereas with uretero-sigmoid anastomoses one loses all control of the situation, and the infections, which are frequent, can not be directly attacked. These implanted sigmoid ureters almost regularly become dilated and infected and the kidneys in turn become hydronephrotic and often pyonephrotic. In some cases the primary dilatation of the upper urinary tract may recede, as demonstrated by excretory urography, which alone tells graphically the fate of these transplanted organs.

With the development of greater interest in total cystectomy, most surgeons in this field have gradually felt their way and determined with some accuracy what cases should be treated by this radical procedure. Quite naturally, as in all developing fields, mistakes are made in determining which cases should be subjected to total cystectomy, and frequently attempts have been made by most of us to remove carcinoma of the bladder which were quite beyond surgical removal. This undoubtedly has contributed to the mortality of the operative procedure, and probably in view of this high published mortality (50 to 60 per cent) many surgeons have refrained from trying total cystectomy when it was indicated and have employed less radical and less satisfactory procedures.

As I have felt my way in this field, I am sure that cases that should have had the benefit of this operation have been widely resected, with disastrous results, and again I am equally sure that I have tried repeatedly the impossible when total cystectomy could not eradicate the disease. In one such case I had to remove the bladder and all the parietal peritoneum with both rectus muscles and fascia as well as the overlying skin up to the navel in order to excise all the apparently involved, indurated tissue. Having started the operation, it was impossible to back out and I had to proceed in the face of such an extensive involvement, realizing that successful removal and outcome were impossible. In this way we gradually acquire sufficient experience and learn to avoid unnecessarily raising our mortality without benefiting the patient. Of my original series of seven total cystectomies with ureter implantation in the skin, I was able to discharge the patients without any mortality, whereas in subsequent years, while testing out the possibilities of this procedure and becoming more and more radical, taking bigger and bigger risks, my mortality has become quite sizable, despite the use of identical or better technique.

INDICATIONS

Infiltrating malignant growths situated at the neck of the bladder, and those involving both ureters, or involving one ureter with extension close to the second ureter orifice, lend themselves to total cystectomy. In addition, there is a group of patients in whom there is a diffuse carcinomatous infiltration of the bladder wall (though the mucosal manifestations may be slight) that demand total cystectomy. These cases of diffuse infiltration are often recognized only at the operating table. Occasionally some of these tumors at the

neck of the bladder do not infiltrate beyond the mucosa and it is possible that less radical treatment than total cystectomy may

Fig. 1. Photograph of patient with uretero-cutaneous anastomosis, ureters intubated with rubber tubes.

be effective; in fact I have seen one such case cured, after reaming out the neck of the bladder with a flexible loop electrode and introducing radium seeds. This case dates back five and a half years. If only one ureter is involved, and the second ureter orifice is not approached by the growth, it has been customary to make a partial resection of the bladder, with transplantation of the ureter, which was involved, into a new place in the posterior wall or the lateral wall of the bladder. The results in these extensive, partial resections have been more gratifying than most surgeons have reported. (Beer, Tumors of the Urinary Bladder.)

It may be proven eventually that not only cases of carcinoma of the bladder are best treated by total cystectomy and partial prostatectomy, but that cases of frank carcinoma of the prostate are best treated by a combined abdomino-perineal complete cystectomy and prostatectomy. At present, the few cases of carcinoma of the prostate which are operated upon radically are done perineally, with the result that the surgeon in traumatizing the tissues is continuously running the risk of forcing carcinoma cells into the circulation and inviting metastases. On the other hand, working against the lymph stream from above down, as in cystectomy, associated with complete prostatectomy, one follows the rational surgical method of attempting to avoid traumatizing tissues and forcing cells into the circulation, lymphatic or venous.

The question has also been raised as to whether cases of multiple papillomata of the bladder should be treated in this way, but it does not seem to me that this procedure is indicated as a primary operation in these cases.

TECHNIQUE

The technique of total cystectomy is not particularly difficult,[4] although the operation is a major procedure to most of the patients to whom it is applied because of their advanced age. The operation is done perferably through a suprapubic incision, extraperitoneally, unless the peritoneum on the posterior surface of the bladder is involved, when a combined intra and extra peritoneal procedure must be carried out. The peritoneum should be regularly opened, so as to inspect the posterior wall of the bladder and allow of exploration of the lymphatic glands in the iliac fossa and the pre-aortic glands, as well as the liver for secondary deposits. If such deposits are recognized, there is doubt as to whether one should proceed with the removal of the bladder, in view of the hopelessness of the case, but because of the complete relief which follows the operation from the excruciating pains caused by cancer of the bladder, many of us feel that despite metastases in the local lymph glands, one is justified in proceeding with a total cystectomy.

With the peritoneum opened, the surgeon is in a position to palpate the bladder and confirm the cystoscopic picture and the biopsy evidence, by recognizing any infiltration of the bladder wall, either limited to the neck of the bladder or ex-

[4] Hinman, F. *Surg., Gynec. & Obst.*, 60: 684-688 (March) 1935.

tending through its various walls or to one or more surfaces of the organ. Some surgeons have advised incising the rectus muscle and sheaths transversely in addition to the suprapubic midline incision. Some have resected the symphysis to get a better approach to the bladder, whereas still others have attacked the problem through the perineum, after temporary resection of the rectum. F. Hinman has recently advocated a retrograde operative procedure. As these operations are liable to be exploratory in character, I would not advocate this technique, as it cuts across the urethra before one has decided on the total cystectomy. All these variants on the simple procedure through a midline, suprapubic incision have never been deemed necessary in our clinic. After the peritoneum has been opened for exploration, it should be closed by suture before the bladder is extraperitonealized, leaving attached to the bladder any peritoneal areas which are involved in the growth. At times it is necessary to open the bladder and inspect its interior to be sure that the cystoscopic and cystographic interpretations have been correct. Occasionally it

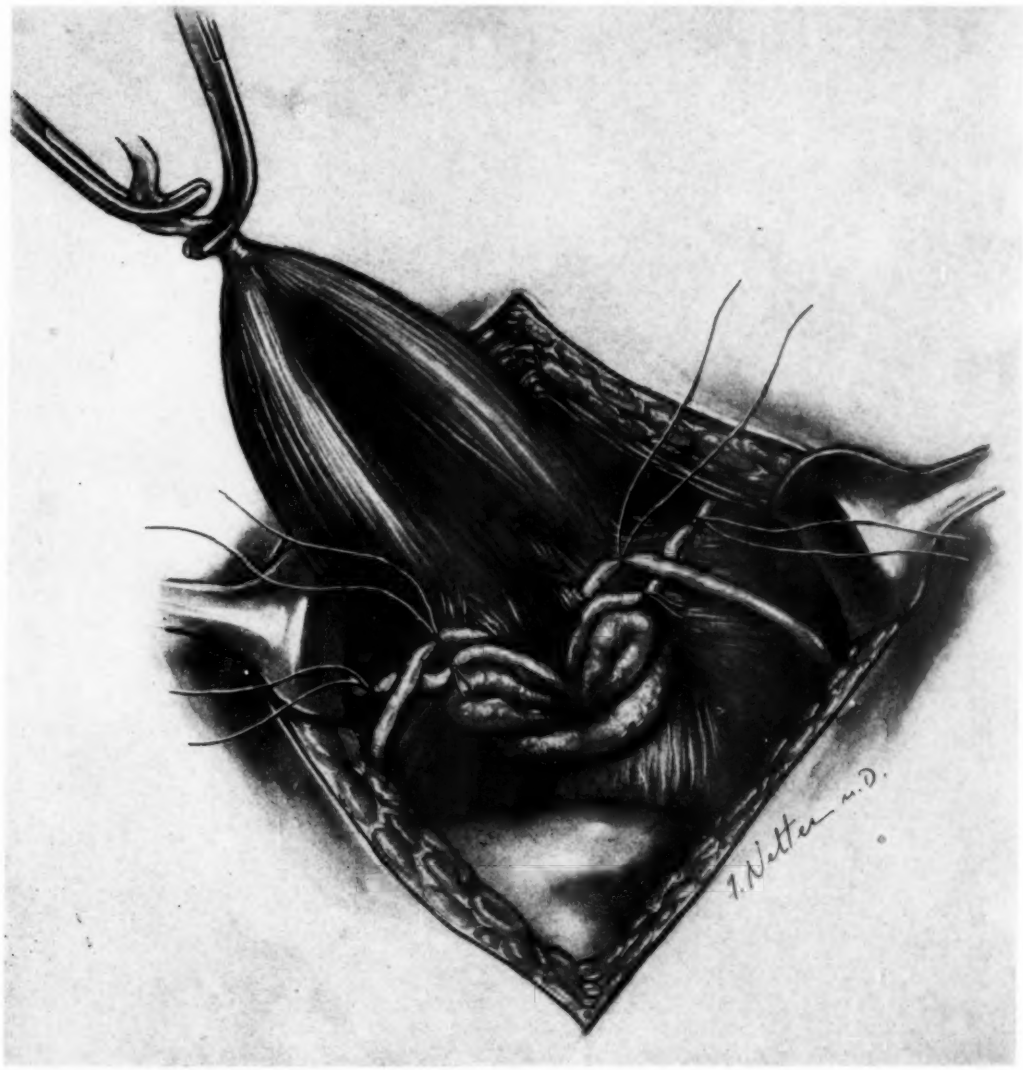

Fig. 2. Diagrammatic representation of the operation of total cystectomy, bladder having been drawn out of its peritoneal covering and completely freed, viewed from the posterior aspect showing ureters, vasa and vesicles, as well as the beginning of the base of the prostate.

may be necessary to do a biopsy of the tumor, or even of the thickened bladder wall, to be sure of the nature of the condition and the extent of the involvement. This may be done by frozen section in the operating room, though at times one may have to delay and get more perfect microscopic control.

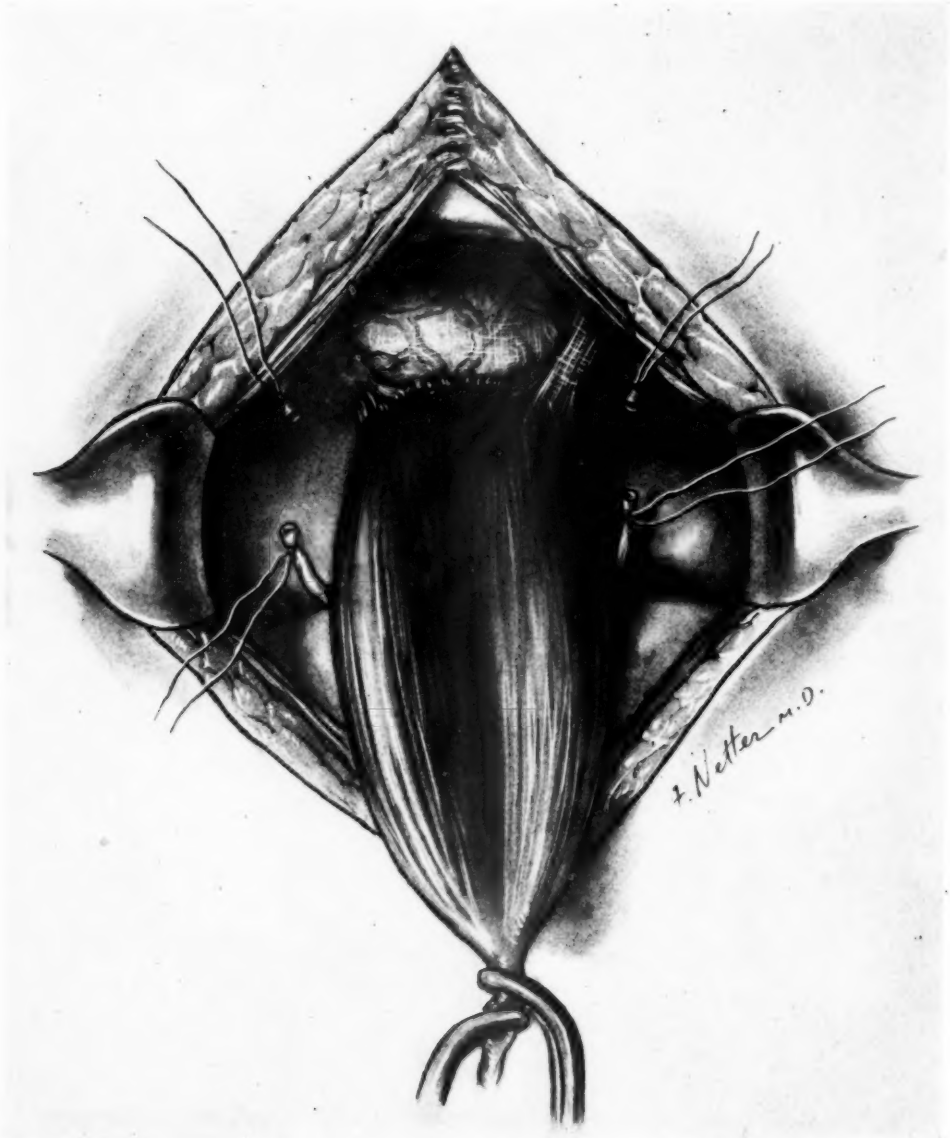

Fig. 3. Appearance of bladder and prostate during the course of total cystectomy, viewed from in front before transfixion stitches have been passed through the prostatic pedicle.

After making a long midline incision over the bladder, which has been thoroughly washed out and emptied, the patient is placed in high Trendelenburg position and with the above reservations (in connection with the exploration of the peritoneal cavity, and the excision of any involved peritoneum attached to the bladder) the bladder is gradually separated bluntly from the perivesical space. The perivesical fat is sponged towards the bladder and the various structures containing the blood vessels are doubly tied on either side, thus disposing of the various vesical arteries and veins. As the bladder is freed in this way, the urachus being held in a strong clamp (which allows the operator to draw the bladder out of its bed) the

vasa are exposed on either side as they cross the ureters, and are tied doubly and cut between.

Having reached in this way the position of the ureters, the latter are freed well down to the pelvis, avoiding exposure of any carcinomatous extension along the ureters. The ureters are doubly tied with catgut and cut between ligatures. The proximal ureter stumps with long ligature attached are covered with saline soaked gauze and dropped back into the pelvis. By these maneuvers one has the whole bladder, seminal vesicles with attached vasa and attached lower ends of the ureters, in one's hand, and with finger tip dissection, one can readily raise the base of the bladder with the above attached organs from the rectal wall, and insinuate one's hand behind the prostate outside of its proper capsule. To mobilize this mass of tissue more completely, one must tear through the pubovesical attachments anteriorly, which is easily done after a few snips of the attachments with scissors, when the hand can be readily passed around the lateral aspects of the prostate. The bladder and prostate are now free, except for their attachment to the apex of the prostate.

Up to this stage, and at this stage, the operation is like a hysterectomy, in that the lateral vessels are sectioned and the whole mass is pedicled on the prostate, instead of the cervix. As the prostate in these carcinomas (especially those involving the neck of the bladder) is liable to be involved to some extent, a goodly portion of it must be removed. To control bleeding from the prostatic plexus, which at times is much engorged, transfixion sutures of heavy silk or chromic gut should be used well down near the apex of the prostate. As soon as these are tied, the prostate should be cut through with the radio knife, without any undue bleeding, the proximal part of the prostate having been clamped to shut off the urethra so that none of the tumor or intravesical contents are squeezed into the pelvic tissues. If the prostate is more extensively involved and has to be removed in toto, it is probably best done through a secondary perineal incision in the lithotomy position, which will allow the operator to expose the apex and cut across the urethra at the level of the triangular ligament, thus allowing complete removal of the prostate with the bladder and its attached organs. In view of the fact that the transfixation ligatures on the prostatic stump in some cases do not completely control the bleeding, the stump must be carefully inspected at this point, as well as towards the end of the operation.

Having removed the bladder and the prostate gland in part or in toto, the disposition of the ureters in the skin has to be taken care of through small grid-iron incisions, about the level of the anterior superior iliac spines, about one inch mesial to them. As there should not be any tension on the ureters, and to avoid any angulation of the ureters in their new position in the abdominal wall, one must free the ureters well into the lumbar region, so that they can be readily swung laterally. Moreover, the peritoneum in the iliac fossa must be dissected and displaced mesial from the position of the grid iron incision in the abdominal wall so that the ureters in their course do not traverse the reflection of the peritoneal cavity, which usually reaches laterally to the position in which the ureters are to be placed. After making a small grid-iron incision in the abdominal wall, the catgut ligature, which has been left long on the proximal end of the ureter, is seized with the forceps, introduced through the grid-iron incision, and the ureter, by means of this ligature, is pulled through. After the ureter has been drawn out through the grid-iron incision, the ligature is loosened, and the ureter wall is seized with a small Allis clamp to steady it. Depending upon the size of the ureter, it is intubated in its new position with an open end catheter with four to six eyes, or a rubber tube, introduced some 20 cm. up the ureter into the renal pelvis. As the ureter is redundant, it can be readily drawn out through the abdominal wall and

at least 1½ cm. of the ureter is allowed to project above the skin, where it is attached with one or two fine silk sutures. A silk ligature is placed around the ureter and its included catheter or tube at a distance from the skin, which prevents leakage alongside of the catheter or tube and apparently leads to a dilatation of the ureter, so that it can be re-intubated with larger tubes or catheters within a comparatively short time. The ureter, attached to the skin with one or two silk stitches, is protected with vaseline gauze, so that no dehydration takes place which might devitalize the ureter stump. This is almost sure to happen if dry gauze is placed against it.

Having disposed of both ureters in this way, the stump of the prostate is again inspected and complete hemostasis assured. In some cases where there is doubt as to the prostatic infiltration, numerous radium seeds are introduced into the cut surface of the prostate. To destroy any implants that may have been spilt, the median wound and its large recesses are carefully bathed in alcohol (50 per cent), the patient being lowered to the horizontal position. After five minutes' exposure to the destructive action of the alcohol, the abdominal median working incision is closed around a cigarette drain with iodoform gauze, which leads down to the prostatic stump, and the parietes are closed with interrupted stitches in layers. In those cases in which the peritoneum has been widely opened, naturally a peritoneal closure precedes the closure of the fascia, muscular and skin layers, provided this has not been repaired before the mobilization of the bladder, which I much prefer.

Post-operative care of these cases must be particularly careful, so that no infection is introduced through the ureter catheters or tubes by irrigation. Introduction of bacteria which have accumulated within the drainage system, is a definite hazard. Aspiration usually suffices to keep the urine flowing, and if injection must be made, the drainage system should be immersed in alcohol and bichloride to sterilize the contaminated ends of the tubes or catheters. Usually, at the end of a week the silk ligatures which fasten the catheters in the ureters, begin to cut through and there may be some leakage alongside of the catheters. This is not alarming and rarely necessitates putting in a larger catheter or tube until ten to fourteen days have elapsed. Though the ureter stump normally remains viable proximal to the silk thread fastened to the catheter or tube, there is always a danger of necrosis, and if such necrosis develops, it is well to defer changing catheters or tubes until fixation of the ureter in the abdominal wall and under the abdominal wall has taken place. At times premature changing of the tubes has dislocated the attachment of the ureter to the parietes, and if a reintroduction of the tube into the ureter is unsuccessful, the ureter may have to be picked up at a higher level and again brought out, as at the original operation, through a second incision at a higher level. The wound leading down to the stump of the prostate closes rapidly as the drainage material is removed, though occasionally there is a disagreeable discharge, which may come from a necrotic piece of the prostate or possibly from a piece of seminal vesicle which was inadvertently left behind.

During the subsequent course, the ureter tubes or catheters will have to be changed fairly regularly, perhaps twice a month, depending upon the amount of purulent discharge or encrustation which develops, and every attempt must be made to keep the urine acid so as to avoid such complications.[5] In a few rare cases where the introduction of the tubes into the ureters has encountered difficulty because of periureteral inflammation and stenosis, it has been necessary to do a unilateral or bilateral nephrostomy.

In females the technique is very much the same, as far as removal of the bladder

[5] Hyman, A. and Leiter, H. E. Care of Bilateral Cutaneous Ureterostomy. *J. Urol.*, 37: No. 3 (March) 1937.

is concerned, and in the few cases reported in the literature (personally I have never had occasion to do one) the procedure is started as a dissection from below the urethra, which is freed up to the neck of the bladder and tied off before the suprapubic part of the operation is carried out. Whether this is really essential and whether one cannot obtain just as satisfactory results by starting with the suprapubic approach—tying off the urethra from above—remains to be seen. The claim is made that there is less spilling of viable tumor cells if the urethra is tied off first. Spilling of such cells must naturally be avoided in both males and females, as a local implant may defeat the whole procedure.

RESULTS

With Drs. A. Hyman and G. Oppenheimer, in my clinic, twenty-four cases of total cystectomy have been done for carcinoma of the bladder (one case was a sarcoma). Of these cases, the first patient to be operated upon had a uretero-sigmoid anastomosis made, as described in my original report, and the other twenty-three cases had uretero-cutaneous implantations at the same time as the total cystectomy.

Of these twenty-three cases, six died following the operation, and seventeen cases survived it. All the operative cases were males, and the longest survival to date is nine years. Four other cases survived respectively eight years, seven years, five and a half years (after five and a half years, autopsy showed iliac gland involvement) and five years.

Of the seventeen cases that survived the operation, twelve subsequently died, six cases within one year of causes unknown, two cases within one and a half to two years, with definite metastases, and three cases of intercurrent complications. One patient committed suicide in the first year following operation.

To determine the results over a five year period following this operative procedure, there are eleven cases available for study with two operative deaths, or 18 per cent operative mortality. Of the nine patients surviving operation (done prior to June 1, 1932), five patients lived five years or longer, and two are alive at present, five years and nine years respectively since the operation. Judging from the above data, the operative risk of this procedure is somewhere around 20 per cent, and if the disease is radically removed, apparently about 50 per cent of the patients surviving the operation live five years or longer.

From the behavior of the cases done since June 1, 1932, it is likely, in view of the wider indications and the more extensive procedures, that the survival rate for five years will probably be less, just as the mortality is greater.

APPENDIX

In view of some of the comments in the literature on the condition of patients after total cystectomy and uretero-cutaneous intubation, the following letter was sent to several patients who had been operated upon in this manner. Two replies are quoted.

"According to modern literature, it is claimed that patients operated upon by the method employed in your case, with implantation of the ureters into the skin, are ostracized from society, are continuously disturbed by urinous odors about their bodies, all of which prevents their living a normal life.

"As my experience seems to be quite the opposite, could I ask you to drop me a line stating your experience, as one who has been operated upon in this manner?"

The first reply is from a patient, I. C. R., operated upon Oct. 22, 1928, at the age of 55 years. (This case was reported as Case VII, in the *Annals of Surgery*, 90: 864–866, November, 1929.) His letter is dated May 29, 1937, and is as follows:

"I am in receipt of your letter of May 26th, and in reply I want to say, that in

my case, modern literature is certainly wrong.

"For a time, after my operation, there were urinous odors, but I have remedied this. Originally I changed my urinal every other day, but now I do not change until the urinal is worn out which is about twice a year. However I change the connections (the Y and the part that connects with the urinal) about once a week, and no one is bothered with urinous odors. Why this should be a fact I do not know but nevertheless it is so.

"About the discharge around the tubes modern literature is almost right, but in my case I have almost overcome this. There is still a considerable discharge, but I have eliminated the odor by changing my dressings daily. Since receiving your letter I have asked a number of my friends if they detect any bad odors coming from me, and in all cases the answers were the same, 'I should say not,' proving that as yet I am not ostracized."

The second reply is from a patient A. S., operated upon April 22, 1932, at the age of 60 years. His reply follows:

"I am more than glad to reply to your letter of June the 3rd in which you inquire about my social experience since my operation.

"Fortunately for the solution of the problem under consideration my activities have been such as to keep me in close proximity to many people. For the past five years I have been serving on the Board of Directors of the . . . and the . . . radio station. At the weekly meetings, I sit with my colleagues for hours. Never have I heard anyone remark that any unpleasant odor proceeded from me. As a matter of fact I asked these men point blank whether they could detect any odor and they all replied negatively. These people are intimate enough friends not to hesitate to state the truth.

"In addition, I attend other meetings, conferences and banquets from time to time to which I am invited and cordially received. In my opinion this matter depends greatly upon the patient and his attending physician. Cleanliness is here a matter of vital importance. My physician, Dr. L., has instructed me thoroughly in the care of my tubes and in the technic of their irrigation. This care requires not more than an average of fifteen minutes a day. I can certainly assure you that if the only objection to my form of operation lies in the possibility of ostracism because of objectionable odors, such objection is absolutely untenable."

TUMORS OF THE TESTICLE

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DIAGNOSIS

DUE to the insidious painless onset of teratoma testis, about 70 per cent of the patients have not sought medical advice until the elapse of four or more months after the enlargement of the testicle was first noticed. This feature of the disease constitutes its greatest danger. Early recognition of the presence of this dangerous lesion allows the application of treatment methods which in their improved state are bringing about a steady increase in the percentage of cures. Raven's[26] description of the course of a seminoma in each of two brothers is a good example of the relation of duration of the disease and extent of metastases to prognosis. The first brother did not seek medical aid until slightly more than six months after he noticed enlargement of the right testicle. In spite of orchidectomy and irradiation, death occurred in two months. Metastases were palpated in the abdomen. Ten years later his brother noticed enlargement of his left testicle. He sought the aid of his physician one month later. Orchidectomy with irradiation was done. Three years later this patient seemed quite well with an apparently good prognosis. Two-thirds of the patients referred to the Memorial Hospital, New York (Dean[7]), had lost an average of six and one-half months as a result of incorrect diagnoses. Seventy-eight per cent already had demonstrable metastases. In most cases the tumor metastasizes very early and progresses rapidly. It is essential, therefore, that every intrascrotal swelling be thoroughly examined to rule out teratoma before any other diagnosis is made.

The first sign in more than three-fourths of the patients is a gradual painless enlargement of the testicle. The enlargement usually progresses steadily, but it is not uncommon for the swelling to be interrupted by a period of quiescence which may last for months and, rarely, for years. Then for no reason, or possibly following trauma, a secondary and more rapid enlargement occurs. With the continued increase in size of the testicle, pain becomes noticeable. Usually, it is first described as a feeling of weight or a sense of dragging in the groin. Later, pain may be felt in the testis. Most patients will also have noticed that the testicle has become firm and elastic or quite hard with differences in density in different parts. Dean[7] has tabulated other initial signs and symptoms that have occurred:

	Per Cent
Swelling and moderate pain	6.0
Swelling and hardness	3.0
Hardness	3.0
Pain in testis	2.5
Pain and swelling in groin	2.5
Pain in abdomen	1.2
Pain in lumbar region	0.8

Loss of weight, swelling of the legs and thighs, and masses in the abdomen are not infrequently described by the patient as associated complaints. Pain in the abdomen or in the lumbar region in Dean's table indicates the frequency with which metastases had occurred before these patients noticed testicular enlargement.

With the growth of retroperitoneal metastases and often before they can be palpated, there will be dull aching pain in the lumbar region on the side of the affected testis, belching of gas after meals, slow passage of food onward from the stomach

and sometimes vomiting. Dull aching renal pain or sharp ureteral colic may occur due to the pressure of metastases upon the ureter. Involvement of the mediastinum or lungs may have become very extensive before the patient notes the chest pains, hemoptysis, and dyspnea which their presence ultimately causes.

On physical examination, though these tumors are seldom tender, care must be taken to use the lightest touch in order not to dislodge malignant cells. Involvement of the skin of the scrotum is a rare and, when it occurs, a very late manifestation. Hence, the scrotal skin is usually seen to be essentially normal and is freely movable over the tumor. It may be red and shiny if the mass is large. The tumor is unilateral and maintains the shape of the normal testis. It is smooth, firm, elastic. Stony nodulations and cystic fluctuations are usually late manifestations. The epididymis is usually distinguishable from the mass and is normal to palpation at first, but later is lost in the enlargement. Rarely an involvement of the spermatic cord gives the impression of a fusiform mass continuous with the enlargement of the testicle. The inguinal glands are only involved if the tumor has invaded the scrotal skin.

It is not uncommon for fluid to surround the tumor. To allow more careful palpation, this should be aspirated but care should be exercised not to puncture the tunica albuginea. The tumor itself will not transmit light. The fluid is usually clear; if bloody, the epididymis is probably invaded.

Rectal examination is usually negative, although in a few cases, a firm rounded mass may be felt above and lateral to the limits of the prostate.

The great majority of tumors appear between the ages of 20 and 40 years, but all ages are affected, including infancy. Mixed tumors are more prevalent in children.

Clinically, there are no specific pathognomic signs or symptoms. The finding of a characteristic metastatic tumor associated with the intrascrotal mass will verify the clinical impression of the presence of a malignant tumor. The primary abdominal metastases are at the level of or slightly caudad to the umbilicus and on the same side as the involved testicle. Being retroperitoneal, they are overlaid by intestine or stomach. If palpable, they are single, firm, round, fixed and not tender. Widening of the mediastinum, hilar infiltration, or metastases into the parenchyma of the lungs require the use of routine roentgenograms to reveal their presence. Metastases to the signal node of Virchow in the left supraclavicular region are easy to detect and should always be looked for because they represent a generalized invasion.

Differential diagnosis involves a consideration of the following conditions which also cause intrascrotal masses:

1. *Gumma.* The gumma is chronic and very slow growing. It is a small or medium sized, very hard mass restricted to the testis. The normal portion of the testis palpable around it does not give the impression of having undergone an atrophic change. Associated hydrocele is usual. There is no fever or pain. Occasionally, there is suppuration, and associated is often a characteristic generalized luetic adenitis. The presence of a positive Wassermann test practically rules out teratoma, but the administration of iodides and mercury will cause a rapid decrease in size of the gummatous testicle in one week, although it will not affect enlargements due to other causes.

2. *Tuberculosis.* The tuberculous testis is usually associated with slight fever and slight pain. There is a marked tendency to suppuration. Often pyuria is present. The epididymis is nodular and adherent. The vas deferens may be beaded. The seminal vesicles are usually nodular and the prostate sometimes presents stony nodules. The tuberculin test is four plus. Confusion is brought about by the fact that the combination of tuberculosis and teratoma is not uncommon. Tuberculosis itself may invade the whole testicle, and conversely, some atypical teratomata will give the same picture as tuberculosis with invasion

of the epididymis, formation of fistulae and perineal scars.

3. *Hydrocele.* There is usually a swelling at the base of the penis giving the impression of apparent retraction. The fluid will transmit light. Drainage by tapping the tunica vaginalis will help the diagnosis by permitting the testis to be carefully palpated. Hydrocele or hematocele may undergo organization and form a hard mass. Hematocele without organization may fail to transmit light. An *X*-ray film taken with a soft exposure may help in diagnosis if the tumor is an adult type of teratoma containing hair or bone.

4. *Old Scars.* There have been a number of cases reported where severe trauma caused so much scarring and distortion of the normal contour of the testis that the nodular formation of a tumor with atrophy of testicular substance was simulated. Carefully studied microscopic sections were necessary to rule out the presence of a new growth.

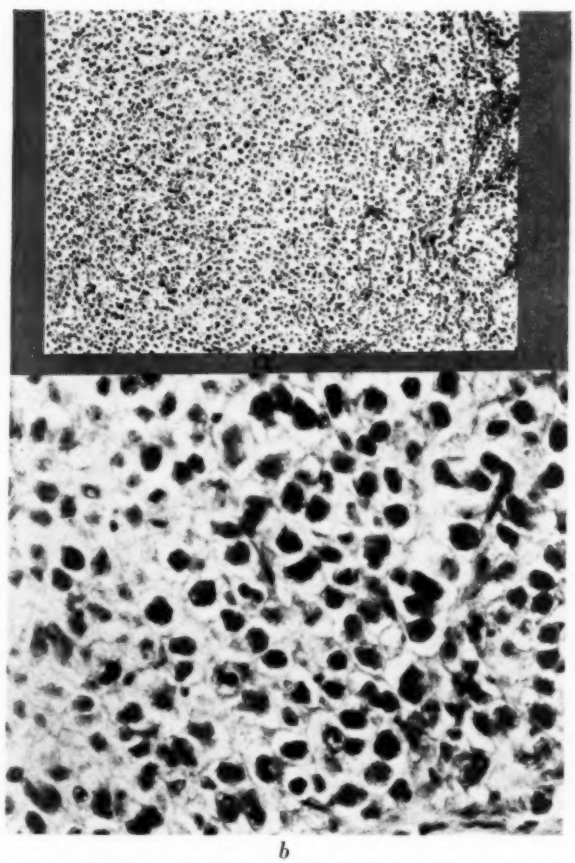

Fig. 1. Photomicrographs of embryonal carcinoma of testis. (*a*) Low power, even distribution of cells with some lymphocytic infiltration. (*b*) High power, reticular type of cells with uniform structure.

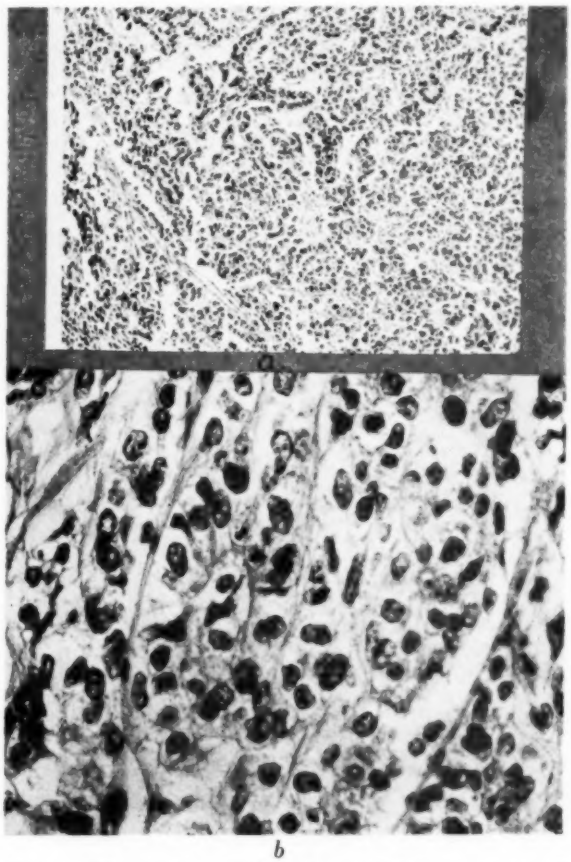

Fig. 2. Photomicrographs of teratoid type tumor of testis. (*a*) Low power, irregular cellular structure, rudimentary acini and fibrous tissue. (*b*) High power, showing anaplastic cells that make histologic determination of radiosensitivity very uncertain if it is attempted before they are irradiated.

5. *Metastatic Tumors.* The testicle may be the site of metastasis from other organs, cells from which have been conveyed here by the blood stream. Such nodules are most often found loosely attached in the tunics, and are easily distinguished from new growths within the testis.

The early diagnosis of teratoma in the cryptorchid is very rare and difficult to make. If the testicle is retained in the inguinal canal, the signs of swelling and symptoms of localized pain will be recognizable earlier than if the testis is intra-abdominal. In the latter case, dragging pain

in the groin, neuralgia-like pains or edema of the leg may be the only signs and may not occur until late in the course of the disease. The percentage of cryptorchids in the general male population is variously reported as being 0.1 to 0.4 per cent of hospital admissions. Yet in this group, from seven to fifteen per cent of the recorded cases of teratoma testis occur. The greater prevalence of teratoma in cryptorchids has raised the question of trauma as an etiologic factor. The effects of compression, muscular pressure, torsion and direct injury have been considered as possible causative factors. Christofferson[5] mentioned that in two of the five patients handled by him, the teratomata became noticeable some time after the testicles had been drawn into the scrotum. Since the spermatogenic cells in all cryptorchids are abnormal, it is generally felt that some other factor than trauma is involved in the production of testicular tumors in these individuals.

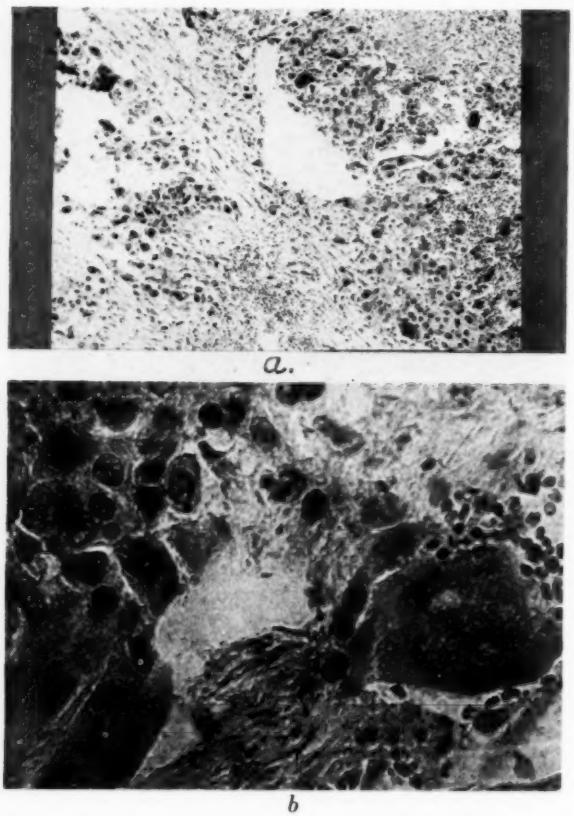

FIG. 3. Photomicrographs of chorionepithelioma of testis. (*a*) Low power, large amounts of necrosis and fibrosis surrounding small area of tumor cells. (*b*) High power, syncyticial cells and free blood.

The discovery that hormones are produced by a large majority of testicular tumors and that these hormones appear in abundance in the urine of many individuals afflicted with these growths has been of the utmost diagnostic importance. The disappearance of these substances from the urine of such patients after treatment has been shown also to have a prognostic value.

The quantitative hormone bio-assay, therefore, becomes an essential diagnostic procedure for teratoma. The test serves three purposes:

1. The quantity of hormone found to be present in the diagnostic test before treatment is started gives some indication of the type of teratoma which is probably present.
2. The bio-assay after initial irradiation will give good indication of the radiosensitivity of the tumor.
3. Repeated bio-assays during and after treatment may be used as the basis of prognosis and will indicate metastases before they are clinically evident if the tumor bearing testicle has been removed.

QUALITATIVE AND QUANTITATIVE HORMONE BIO-ASSAY

The following technique which is essentially similar to that in general use is as given by Ferguson:[10]

When the hormone is not known to be present, a qualitative bio-assay is done with the unaltered morning urine. Measured amounts of urine of 0.2, 0.4, 0.8, and 1.0 c.c. are injected into members of a group of 19–21 day old mice five times during forty-eight hours. The mice are examined in one hundred hours. Should any mice show a positive reaction, a quantitative test is run on another group of mice using twenty-four hour urine which is diluted so as to obtain a close reading on the minimal amount of urine necessary to cause the reaction.

If the first tests are all negative, the hormone is concentrated by Zondek's alcoholic precipitation method and injected

into another group of mice. This is equivalent to five times the amount of unaltered urine. A control animal is examined at the beginning and end of every test as a check on the normal changes that may occur. Owen and Cutler[35] recommend the use of the Doisy-Katzman's benzoic acid concentration method in preference to the Zondek alcoholic extraction. This is slightly more accurate and is of special value in removing toxic materials that may be in the urine.

The animals are examined grossly and microscopically. A characteristic of this hormone is that it causes the uterine horns of the mice to become markedly enlarged, edematous, clear and colorless. This was first observed at the University of California Clinic, and is now used almost exclusively by Hinman[19] in reading the test. The ovaries are examined with hand lens and microscope. The hormone may cause three reactions in the ovaries, as noted by Zondek:

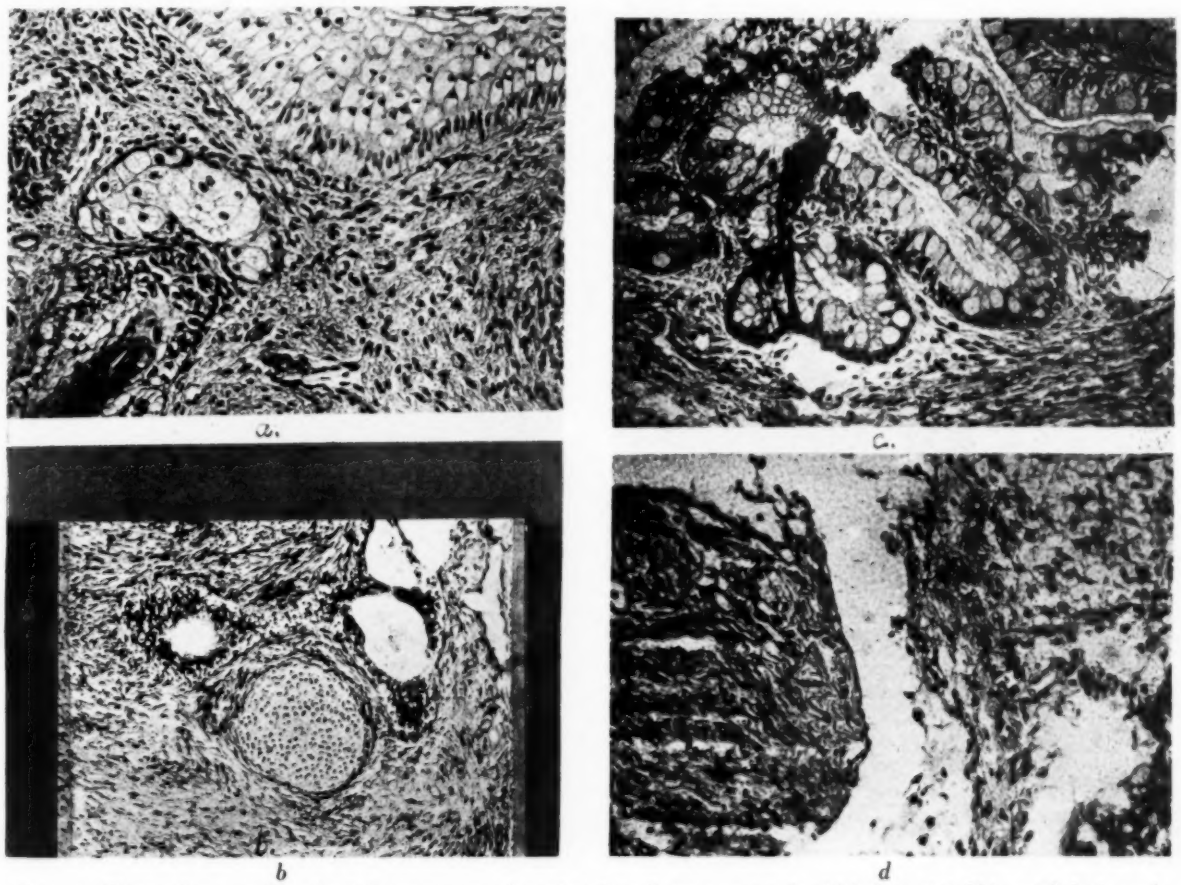

FIG. 4. Photomicrographs of adult teratoma of testis taken from 11-month-old infant. (*a*) Skin with hair and sebaceous gland; (*b*) cartilage and mucous gland; (*c*) intestinal mucosa with goblet cells; (*d*) smooth and striated muscle and central nervous tissue.

Reaction I: Immature follicles become mature.

II: Follicles become hemorrhagic forming the "blood points" which are easily visible with hand lens.

III: Luteinization reaction with formation of atretic corpora lutea.

The hormone is estimated in terms of mouse units. One mouse unit equals the smallest dose of urine, expressed in c.c., that produced definite ripening of the follicles or unmistakable enlargement of the uterine horns when injections are given five times in forty-eight hours, and the animal is killed in one hundred hours. This

unit divided into 1000 equals the mouse units per liter.

Many times there is enlargement of the uterine horns with no demonstrable stimulation of the follicles. Reactions I and II usually occur together, but Reaction III seems to be caused by a separate factor in the hormone that is not always present. Ferguson[9] considered the hormone, causing Reactions I and II, as being prolan A from anterior pituitary and thought that prolan B caused Reaction III. If Reaction III was present, he calculated the quantity of hormone present by multiplying the mouse units per liter by five. However, Freed and Coppick[13] and Hinman and Powell[25] have shown that the hormones of pregnancy and of testicular tumors are identical in all physiological reactions, and reveal certain definitely different physiological reactions from the anterior pituitary hormone. Hamburger[14] and others have shown that in pregnancy there is no constant ratio between the follicle stimulating dose and the luteinizing dose. In this respect it is similar to urine from patients with testicular tumor. The Aschheim-Zondek test will not differentiate anterior pituitary and teratoma hormones.

The quantity of hormone excreted per liter of urine closely parallels the rapidity of growth and the degree of radiosensitivity of the tumor. Comparison of the pathology of the tumors and the hormone output has lead to the consideration of five general groups.

The studies of Dean[7] and Ferguson[10] at the Memorial Hospital, New York, give some slightly different results from those obtained by Owen and Cutler[24] at the United States Veterans Facility, Hines, Illinois. About an equal number of patients is represented in each group.

The hormone output is increased in proportion to the extent and growth of metastases, but the increase is less than that caused by a higher grade of malignancy, and generally remains within the range of its group.

Dean and Ferguson	Owen and Cutler
1. Negative Test	1. Negative Test
(a) No teratoma.	
(b) Adult teratoma which has not destroyed all the interstitial cells.	
2. 500 m.u./liter or less.	2. 0–400 m.u./liter—average 100
(a) Adult teratoma.	
(b) Early small tumor of low grade malignancy that has not destroyed all interstitial cells.	
(c) Syphilis, tuberculosis, or interstitial orchitis that caused swelling and destroyed interstitial cells.	
Tuberculosis after invasion of the testicle presents a very difficult picture to diagnose. Records disclose the not rare presence of tuberculosis and teratoma.	
3. 500 to 2000 m.u./liter	3. 100–200—average 200
Probably a seminoma.	
4. 2000 to 10,000 m.u./liter	4. 200–5000—average 1500
Embryonal cancer with lymphoid stroma.	
5. Over 10,000 m.u./liter	5. 1000–20,000—average 7000
Embryonal adenocarcinoma.	
6. 50,000 up to 1,000,000 m.u./liter	6. 10,000–125,000 plus—average 60,000
Chorionepithelioma.	

As in all laboratory tests, this has its limitations. Owen and Cutler[23] noted the following limiting factors after making quantitative hormone tests on the urine of many male patients including 125 cases of suspected teratoma:

1. The Friedman virgin rabbit test requires a minimum of 2000 m.u./liter for positive reaction.

2. The immature mice give the most easily read reactions.

3. The morning urine generally contained more hormone than did the twenty-four hour output. Hence, fractional parts of the latter should be used for quantitative tests. The total daily output varied but little.

4. The following conditions showed an increased output of hormone:

Castration

Increased intracranial pressure

(a) Cyst of testis up to 400 m.u./liter.

(b) Granuloma up to 500 m.u./liter.

(c) Epididymo-orchitis up to 200 m.u./liter.

5. False positives occurred in less than 10 per cent of the cases of suspected teratomas.

The three cases, a, b, and c, above, showed persistent gonadotropic hormone output in repeated bio-assays. Other patients with similar diseases did not produce the hormone. This, apparently, is due to an imbalance between the remaining testicle and the pituitary and as in castrates, the hormone is from the anterior pituitary and is not the hormone of teratoma or pregnancy.

Dean[7] has noted in following up some teratomatous patients who had orchidectomy or intense irradiation that the hormone output will vary from 0 to 2000 m.u./liter over a period of years, although the patients are clinically in good health and show no signs of the presence of teratoma. This is also probably due to imbalance between the irradiated or the remaining testicle and the pituitary. Animal experiments show that this hormone is identical to the anterior pituitary hormone and differs from that of teratoma or pregnancy. Owen and Cutler[24] noted that two-thirds of acromegaly cases produced gonadotropic hormone in urine.

Hinman and Powell[19] feel that the presence of less than 300 m.u./liter of hormone does not denote either presence or absence of teratoma. They believe that the concentration method is rather inaccurate, and a finding of 150 m.u./liter should be interpreted as being from 100 to 300 m.u./liter. The fact that there is a cyclic appearance of the gonadotropic hormone in normal men, that an embryoma elsewhere in the body, and other conditions, also produce a small amount of hormone, rules out the value of bio-assaying the concentrated hormone. They have been using a simplified and much more rapid test at the University of California Clinic. The first injections will give positive readings from 300 to 3000 m.u./liter. The interpretation is based mainly on the macroscopic examination of the reaction in the uterine horns. The ovaries are inspected with a hand lens, and if the corpora lutea or hemorrhagic cysts are seen, a new group of animals is injected with smaller doses to determine the smallest dose which will cause the uterine reaction. A test reading below 300 m.u./liter is called negative.

Ferguson has never had a case of teratoma from which no hormone was obtained. Hinman has had three cases of seminoma and two cases of adult teratoma from the urine, of whom serial bio-assays were always negative. Whether or not he used the concentration method he failed to state. Judging by Owen and Cutler's figures at Hines, where the concentration method was used, some adult teratomas may give absolutely no hormone and some of the seminomas may secrete less than the 300 m.u./liter used as a minimum by Hinman. Since adult teratomas form less than 10 per cent of all teratomas, the hormone bio-assay has been diagnostically positive in at least 90 per cent of the cases.

There is one limitation to the hormone bio-assay which must be borne in mind. The quantity of hormone excreted indicates the general type of teratoma that may be present. This also agrees with the radiosensitivity of the tumor. If a "therapeutic" dose of irradiation given to a primary tumor without evident metastases causes a decided drop in the hormone output, the prognosis is considered good with irradiation therapy. It has been shown, however, that two other factors may be present. (1) The hormone output has completely disappeared from some tumors after irradiation but active malignant cells remained and caused extensive metastases. These cells had probably already invaded the lymphatics. The hormone later increased greatly. (2) Pathological examination of some other primary tumors which metastasized after there had been an apparent complete response to irradiation, disclosed that the tumor was a mixed type with adult radioresistant cells remaining after the embryonal cells had become necrotic due to intensive radiation therapy.

HISTOLOGIC DIAGNOSIS

Histologic diagnosis may be used as a primary diagnosis, or is of decided value in

determining the degree of radioresistance of the tumor after the initial hormone test and irradiation is completed. Since any trauma to the testicle must absolutely be avoided, the microscopic study is limited to that obtained by complete orchidectomy whether it be done before or after irradiation.

A properly performed biopsy is a decided aid in making an early diagnosis. Whenever a testicular tumor is suspected, the tunica albuginea should never be incised or unduly traumatized. Dean,[7] however, has found that a biopsy can be safely aspirated through an 18-gauge needle, and a histologic report obtained in ten minutes. This should only be done if intensive radiation is available for immediate use should the report be positive.

Hinman[17] feels that a histological examination is necessary immediately whenever there is suspicion of teratoma in an enlarged testicle. Orchidectomy, he believes, involves no risk when incision is made at the external ring and the cord clamped there before the scrotum is touched. If the testicle is found to be tuberculous, luetic, or the site of another form of epididymo-orchitis, its loss is negligible. Since the hormone is in the hydrocele fluid and in the tumor itself in at least five times the quantity found in the urine, a large part of the testicle is placed in acetone for extraction of the hormone. In this way the histologic classification of the teratoma may be aided by the quantity of hormone found, and a better idea of radiosensitivity is available.

Randall and Bothe,[25] Dean,[7] and others strongly object to this approach. Metastases may be present and their growth is likely to become much more rapid following removal of the primary tumor. Orchidectomy, in their opinion, should always be withheld until the full effects of irradiation are received. This is usually about five to six weeks after irradiation was started. This is termed the therapeutic or diagnostic irradiation. Fifteen hundred to two thousand units are given in three hundred to five hundred Roentgen doses over a period of five days. The complete effect is noted by measuring the decrease in size of the testicle with calipers, the maximum decrease being reached in four to six weeks. The hormone output may disappear or decrease to a maximum degree immediately upon completion of the irradiation before the testicle has decreased in size. Any delay in diagnosis caused by relying on the completion of the hormone bio-assay is more than compensated for by the greater safety in using irradiation before performing orchidectomy. As an additional safety factor, these authors recommend that irradiation be started at the neck and worked toward the scrotum. This is to control any metastases that may be present and to prevent possible cell dispersion from the primary tumor under initial heavy irradiation.

Orchidectomy is indicated in the presence of the clinical picture of teratoma when the hormone bio-assay is negative or a very low positive. Early orchidectomy in such cases would be done with the hope of preventing metastases of such a radioresistant tumor, the histologic diagnosis being secondary. Most clinicians think that histologic examination of the testis after irradiation gives decidedly more definite and specific information for diagnosis of the type of tumor and prognosis than can be obtained by examination before irradiation.

The histologic classification of tumors of the testicle has now resolved the former specific multiple grouping into four general groups which are correlated with the extent of their ability to generate the hormone.

That these groups are not well delineated, except in the case of the complete adult teratoma, is borne out by the admission on the part of the pathologists themselves that their judgment of the radiosensitivity of the tumors they examined was wrong in at least 50 per cent of the cases. This variegated cellular structure of the tumors agrees with the opinion expressed by Ewing in 1911. His studies indicated that all these tumors were tera-

tomatous and arose from totipotent sex cells. One germinal cell growth may predominate and outgrow the others in any tumor. The proportion of radiosensitive embryonal cells and the more differentiated radioresistant cells must, therefore, be determined for each tumor. Maner,[21] after the difficult task of examining multiple sections of seventeen testicular tumors, confirmed this induction. Seven of the seventeen tumors were so-called seminomas. Two or three primary germ layers were found in sixteen of the seventeen tumors. Primary germ layers were not found in one seminoma. On the other hand, the characteristic seminoma cells were found in fifteen of the tumors. Sections of one of the tumors revealed the picture of a benign adult teratoid tumor, but a retroperitoneal metastasis contained malignant glandular and seminoma cells. The histopathologic picture showed marked variations in the types and in the quantities of the cellular constituents of each tumor.

Because of this mixture of embryonal and differentiated cells, it is seen to be hazardous to determine the type of treatment and make a prognosis on the microscopic study of the untreated tumor, unless it should be one of the uncommon adult teratomata or the very rare chorionepithelioma. Irradiation will make marked changes in the embryonal cells and destroy most of them so that the presence of the differentiated radioresistant cells is more evident. The following classification includes the macroscopic and microscopic anatomy of the tumors before and after irradiation:

I. Embryonal tumors

Form 90–95 per cent of the tumors of the testis.

A. Embryonal carcinoma

Figures 1A and B.

1. Gross: Firm with cartilaginous consistency.

Cut surface: homogeneous, cream colored, firm and fleshy. There may be fibrous septa.

2. Microscopic:

(a) Small cells with well marked lymphoid stroma forming distinct strands.

(b) Majority have larger, pale staining cells with varying amounts of lymphoid stroma. These are usually called seminomata.

(c) Typical seminoma with large, vesicular, oval or round cells resembling spermatocytes that form structures resembling a rete. The nuclei are reticular. The cells are not closely packed, and a section reveals a uniform areolar-like net of similar cells. Lymphocytes commonly infiltrate in several areas. These tumors elaborate much less hormone than (a) or (b), averaging about 200 mouse units per liter.

(d) Included in this group is the occasional tumor with large primitive cells which are pale staining and reticular. The hormone output equals that of chorionepithelioma, but the syncyticial cells which characterize the chorionepithelioma are not present.

B. Mixed embryonal teratomata

Figures 2A and B.

These tumors contain a much higher proportion of the three primitive germ layers.

1. Gross: Firm, hard, possible soft cystic areas.

Cut surface: Irregular growth of fibrous tissue, separating glandular and cystic areas. Color is pale, creamy in some areas and dark and vascular in others.

2. Microscopic:
   (a) Marked teratoid type: Mostly differentiated cell layers, with some primitive cells and areas of adenocarcinoma scattered through irregular strands of fibrous tissue. Most of the cells will be hyperchromatic and dark staining.
   (b) Adenocarcinoma: Closely packed, hyperchromatic, dark staining cells with the appearance of acini and ducts separated by fine connective tissue fibers. It is common to see complete necrosis in parts. (a) and (b) are not separate entities, but merely express the varying degree of differentiation of the cellular structure. The anaplastic darkly staining cell predominates in both types, and a higher proportion of radiosensitive cells occur in (b).
   (c) Chorionepithelioma: Figures 3A and B. Very irregular growth of the tumor with lobulated outline. Typical syncyticial cells and villi similar to those occurring in women.

II. Adult teratomata
Figures 4A, and B, C and D.
Form about 5 per cent of all testicular tumors.
A. Gross: Hard, firm tumors, frequently with soft areas due to cysts. Cut surface: variegated heavy connective tissue septa with pale cellular areas interrupted with many cysts of various sizes.
B. Microscopic: Fully differentiated adult type of active glands, squamous epithelium, and possibly bone or hair. Malignant cells scattered between the adult structures.
Irradiation produces but little change in these tumors. A few areas of necrosis may be found but the malignant cells are not destroyed in any great number.

III. Miscellaneous tumors
Form 1–2 per cent of testicular tumors. Except for the rare sarcoma, they are usually benign and clinically unimportant, except as a diagnostic hazard.

The microscopic study of the primary tumor after the initial irradiation is of great clinical importance and is a guide to prognosis and subsequent treatment.

The radiosensitive tumors all present the typical picture of destruction of the tumor cells forming a uniform necrotic mass or areas of cell free reticulum. Dean[7] stresses the importance of recognizing the following reactions:

A few undergo general necrosis leaving a mass of shadow cells enclosed in a relatively avascular capsule. Diagnosis of embryonal carcinoma can be made at this stage by the arrangement of the shadow cells. Later, the mass becomes homogeneous and caseous-like. This has not infrequently been mistaken for a gummatous testis.

In some of the tumors, damage to the blood vessels with hemorrhage converts the growth into a characteristic hematoma with the additional necrotic changes from irradiation.

A third group present a "more complicated picture of a loose fibrous reticulum, poor in cells." The spaces are the site of former tumor cells, and more peripherally, of testicular tubules. These tubules may have been lined with tumor cells. A thick, homogeneous, hyalin membrane surrounds the spaces. "An occasional hydropic degenerated cell, unidentifiable as to type, may be seen lining this membrane. A few lymphocytes are found in some of the interstices of the spongy, coarse retic-

ulum." Later productive fibrosis increases and obliterates the spaces with the deposition of calcium salts in some. The end-result of all these reactions is probably cicatrization and formation of a relatively avascular hyalin scar.

The radioresistant tumors, embryonal teratoma, present a more varied picture as a result of the irradiation. In some, most of the cells may be embryonic and completely destroyed with active malignant cells scattered in groups throughout the field. Later, the recurrent growth invades the diffuse mesh work of necrotic cells or in some, where there was great necrosis, the recurrent growth spreads at the periphery.

It is important to observe the periphery of these tumors especially toward the upper pole. Remains of the testis proper, if present, are usually encountered here. When the testicular remains are separated from the neoplastic growth by heavy fibrous tissue, there is justification in presuming the presence of a teratoid type.

Treatment by either irradiation or surgery is directed to the prevention or control of metastases which usually follow the course of the lymphatic drainage. The rapidly fulminating and wildly malignant chorion-epitheliomas and some of the adenocarcinomas may metastasize very early via the blood stream. These metastases are usually widespread through most of the organs of the body. These are the types which frequently metastasize to the brain.

The lymphatic drainage follows the spermatic cord and goes directly to the retroperitoneal glands in the lower part of the abdomen at about the bifurcation of the aorta. Here are the primary groups of glands. Each testicle has its own group of glands located on its own side. These glands intercommunicate and receive efferents from other locations. The primary group drain into the intermediate secondary nodes which are para-aortic to a level about 2 cm. above the renal pedicle. The secondary nodes are in the mediastinum, hilar region of the lungs, and Virchow's node. Involvement of Virchow's node usually denotes general metastases.

Although the primary metastasis is on the same side as the tumor, it may quickly involve the glands of the opposite side. It is generally stated that the metastases to the chest occur quite early. A study of case histories, however, indicates that such judgment was based on the time of the clinical appearance of abdominal metastases and upon necropsy reports. In those cases in which orchidectomy is done early in the course of the disease, it can be seen that abdominal metastases which are not recognizable clinically are often present relatively soon after onset. Usually, the chest metastases do not appear for a considerable time. If the patient has had a course of irradiation, the mediastinal involvement may not appear until a recurrence sets in some time after treatment. In those patients whose first treatment is delayed, it should always be assumed that tumor cells have probably reached the mediastinum.

In some necropsies, a lymph channel has been demonstrated ascending directly from the lower lumbar to the mediastinal glands without intermediate nodes. The only conclusion that can be drawn is that proper treatment by irradiation should always include the chest regardless of the evidence of the presence or absence of metastases in that region.

Chorionepithlieoma form about 1 per cent of the teratomata. They show wide variations in rapidity of growth and duration before diagnosis is made. The duration from onset to diagnosis has varied from four months to two years. They are very radioresistant and death usually occurs from multiple blood stream metastases. The high amount of hormone elaborated is usually diagnostic. Gynecomastia occurs and is an early indication of the disease.

Craver and Stewart[6] described a case of chorionepithelioma in a 15-year old boy where both testicles were atrophic. The only complaint was dyspnea and pain in the chest. Death occurred in three months

from general blood stream and lymphatic metastases. Autopsy revealed a small focus of choriomatous growth in the left testicle. Occasionally, the original focus in the testicle apparently heals by sclerosis after metastases become active, and a testicular tumor, the usual sign of teratoma, is missing.

Bilateral involvement occurs in approximately 1 per cent of the cases. Diagnosis should not be misdirected. Teratoma should always be ruled out first. The writer treated a very rare case at the United States Veterans Facility, Sawtelle, California. Seminoma in the patient's right testicle had been treated with orchidectomy and irradiation. There were no evidences of metastases. After thirty months, with no signs of the disease, the patient returned to the hospital with enlargement of the remaining (left) testicle. After castration the patient did not return for irradiation. Both tumors were seminomas with similar histologic structure. Death occurred one year later.

TREATMENT

The prognosis and treatment, considering that the diagnosis is established by hormone bio-assay, depends on the

1. Duration of time between onset of the neoplasm and the start of treatment;
2. Presence of metastases, biologically evident after orchidectomy or clinically evident;
3. Radiosensitivity as judged by the effect of irradiation on the size of the tumor, and on the change in quantity of hormone excreted, and judged by microscopic evidence of viable malignant radioresistant cells in the irradiated testicle.

The element of elapsed time from onset to start of treatment is a great factor in prognosis, and in determining the type of treatment. When proper treatment is delayed until six months or more after onset, records show that metastases are present in practically every case, although many gave no clinical signs or symptoms. A few adult teratomata have been the exception in not having formed metastases in that time. Orchidectomy is of secondary consideration, and intensive irradiation from the chin to the scrotum in repeated courses is mandatory. It can only be hoped that the prognosis which is naturally questionable or poor at the start may become fair, or in rare cases good, under careful treatment which includes faithful observation of the patient after the courses of irradiation.

The treatment of teratoma testis by simple excision, later by radical lymph gland removal, and more recently by irradiation, has paralleled that of other types of malignancy. Teratoma testis has several characteristics that markedly influence therapy and distinguish it from other malignancies. Complete excision of the primary tumor by orchidectomy is simple and easily done. The great majority of testicular tumors are very radiosensitive. Many have been caused to disappear, some apparently permanently, by *X*-ray treatment. The first metastases of most of such tumors are, then, the lymphatics and are limited to the course of the retroperitoneal para-aortic glands and their drainage into the mediastinal glands. This greatly facilitates the administration of direct irradiation to all the secondary growths in most of the patients. Ninety-five per cent of the tumors secrete the gonadotropic hormone whose presence in the urine is telltale evidence of the activity of the primary or metastatic growths.

As the value of irradiation has become known, many patients are being referred to the larger clinics. In the last few years these clinics have written many papers on the treatment used and the subsequent condition of the patients. In studying these reports it is difficult to make a true evaluation of the results of the different methods of treatment. The presence or absence of metastases, the duration of the disease before treatment, and the percentages of radioresistant and radiosensitive tumors in the various groups should be clearly indi-

cated in such reports before statistical studies can be made of them.

There is at present no accurate knowledge as to the very early course of this malignancy. The time of onset depends on the patient's awareness of the presence of the first vague sign or symptom. The duration of the disease from the stated onset to the time of first examination varied from three weeks to five years. Teratoid metastases were present in the patient with the onset at three weeks and death occurred in one year. In instances where teratoma testis afflicted more than one member of a family, the second victims, being more alert for the pathologic changes, sought medical aid within three to five weeks and were cured without any evidence of metastases.

More than one-half of the cases with duration up to five months had metastases. Summarizing the case reports of the past five years disclosed that about 65 per cent of patients with duration of three months or less were cured for three or more years. Mortality greatly increased in patients with longer duration. Thus a long duration is seen to contraindicate radical surgery.

SIMPLE ORCHIDECTOMY

Simple orchidectomy orginally was the usual method of treating these tumors. Unfortunately it continues to be common practice in spite of the knowledge gained during the past fifteen years. Desjardins[8] and Smith[27] report that about 50 per cent of the patients in their clinics who were treated by simple orchidectomy before elapse of six months from onset survived, showing no metastases. The point that should be noted is that, of the other 50 per cent, all developed metastases and all died with an average survival period of only five months. It is of significance that it is very rare for any patient to survive when simple orchidectomy is relied on after six months from onset. Of all patients so treated, only about 6 per cent recovered. The physician using simple orchidectomy is ignoring the presence of silent and unknown metastases which later develop and cause speedy death. It is now a simple matter to send the patient's urine to the nearest laboratory for bio-assay before and after orchidectomy as a verification of the diagnosis and as a means of searching for a sign of the presence of metastases. It is essential that these patients be followed up periodically and carefully watched for signs of recurrence.

Surgical Removal of Teratomal Testis: Whether orchidectomy is performed before or after irradiation, the greatest care should be exercised to avoid starting the migration of any malignant cells along the spermatic cord. Before the cord or the testis may be touched, an incision should be made over the external inguinal ring and the cord clamped immediately. It should then be ligated and severed with cautery. The teratomatous testicle should be gently removed with the tunica albuginea intact. The incision should reach down the side of the scrotum, so that the tumor can be removed without exerting any pressure upon it.

In 1921, Barringer and Dean[2] in treating operative and non-operative teratomata with radium, noted the decidedly curative effect of radium on the "embryonal" type in contrast to the poor or apparently complete lack of response of the "teratoid" and "adult embryomas." This foretold the subsequent swing toward the general use of the Roentgen ray in the treatment of all these neoplasms. The radical operation of Chevassu and Hinman simultaneously has undergone a sharp decline as the method of choice. It is possibly now being too empirically avoided. Unquestionably, there is still an indication for its use.

Irradiation is of necessity the treatment of choice. The early case of radioresistant teratoma may prompt the advisability of radical surgery. But the initial "therapeutic" test of irradiation is necessary in every case. Irradiation is applicable at any stage of the disease. Although its

effectiveness is decreased or slight in the radioresistant tumors, it has caused remarkable improvement in cases with massive, radio-sensitiveness metastases. Its unrestricted field of possible effectiveness and its conservative nature have resulted in irradiation becoming the choice of treatment in nearly every case. In treating all types of teratomas by radiation, Dean[7] has obtained five-year cures in 29.9 per cent.

There is one deceptive characteristic of teratomata which have been irradiated. Many of them become latent and give no signs of their presence for several years. A small quantity of hormone may or may not be excreted. Recurrences have suddenly appeared two to eight years after orchidectomy and irradiation. Prognosis, accordingly, is relative to the immediate progress of the patient, and cannot be considered final in many cases. Five-year cures are not the true end point, and must be considered merely as a convenient basis of comparison of the results of treatment.

There are two opinions of the place occupied by orchidectomy. Since the hormone bio-assay is diagnostic of more than 90 per cent of teratomata, orchidectomy before irradiation is needed only with the occasional case that produces no gondotropic hormone. The value of the histologic evidence of the degree of radiosensitivity after the tumor has been subjected to Roentgen rays is more direct for prognosis and treatment. Randall and Bothe[25] found that there were fewer recurrences and that less patients had metastases in the chest among those who received pre-operative irradiation than among those who had orchidectomy first. Adair[1] reported that Ferguson has had 52 per cent three-year cures since adopting this procedure. Many of those who had orchidectomy first, delayed submitting to irradiation later. In these patients local recurrences in the operative wound are common. Pre-operative *X*-ray should, accordingly, be considered a desirable safety factor.

On this reasoning, the following treatment is indicated when no clinical metastes are evident:

1. The diagnostic hormone bio-assay is completed.

2. The abdomen, including the epigastrium and pelvic region and the testis, is irradiated. If the onset was more than three months earlier, it would be much safer to expose the chest also.

3. The testis is irradiated more intensely than the other areas, receiving five hundred roentgens in each of three treatments in five days.

The object is to obtain a better idea of the radiosensitivity of the tumor by causing as rapid regression as could be safely obtained. The testis is measured with calipers at intervals. If the tumor is radiosensitive, decrease in size is prompt and it returns to very nearly normal size in four to six weeks.

4. Orchidectomy should than be done.

If the tumor does not reduce in size in two or three weeks, it should be removed at once as a radioresistant tumor. In some cases, radiation produces a hematoma which prevents regression in size. It is felt by some that as long as radiation is available, it is unnecessary to remove a radiosensitive tumor. Some such cases are among the five year cures, but many have died with recurrences. Although the proper Roentgen ray dosage should destroy most or all of the growth, there is no clinical test to establish the true status of the tumor and there is no assurance that the patient will continue the repeated irradiation necessary in such cases. Subsequently, if after being negative, the hormone test again becomes positive, it must be assumed, for the patient's good, that metastases are present; the chest and abdomen then must also be radiated. Should he continue the treatment, the spermatogenic function of the other testis will be destroyed. The conclusion is that orchidectomy is mandatory in the complete treatment.

5. Hormone bio-assays are done at intervals of three to six months to detect activity of recurrences.

6. Repeated treatments with irradiation should be carried out if the bio-assay is positive. The ultimate prognosis of these cases depends on the subsequent appearance of metastases. If it was found that the primary tumor was radiosensitive, the prognosis is good. Later, if metastases appear to be present by the positive hormone test, radiation must include the neck and chest as well as the abdomen. The future course determines the prognosis. Many radiosensitive metastases in the chest and abdomen are cleared up by proper irradiation. There exist a few known survivals of eight years and longer. If the tumor is radioresistant, the first prognosis is influenced by the duration of the tumor before treatment was started, as has been stated.

The early cases of less than three months duration may be free from metastases and may be completely cured. The prognosis is poor if the tumor is an adult teratoma. Excision very soon after onset before metastases have occurred, or an early Hinman operation are the only known cures. Irradiation has but very slight retarding effects on this type of tumor.

When metastases are known to be present, the patient must be irradiated from the chin to the level of the great trochanters; the scrotum must be included if orchidectomy has not been done. Orchidectomy should be secondary in such cases. In addition to the initial complete irradiation of the chest and abdomen, irradiation over the metastatic area in the abdomen should be repeated every six to eight weeks. Later radiation of the chest and entire abdomen may be indicated in four to six months.

Smith[27] and Randall and Bothe[25] stress the necessity of radiating the patient from the chin to the inguinal region whenever the biologic test shows the presence of metastases. If metastases happen to be present in the chest, they may thus be brought under early control or possibly completely devitalized. Such radiation may prevent the local irradiation of the abdominal metastasis from dispersing malignant cells under the initial radiation. Perusal of the individual cases of teratoma presented in the various journals substantiates this reasoning, for many cases succumbed with chest metastases which appeared after local irradiation had caused the disappearance of all signs of abdominal recurrences.

The final and important step is the faithful follow-up of these patients after irradiation. Unfortunately, many patients in whom irradiation caused the complete regression of all clinical and biological evidence of metastases, are not heard from until they return in a few months to a few years with palpable metastatic masses. This changes an original prognosis of good or fair to poor. The value to the patient of periodic examinations by means of hormone bio-assay is dependent upon the type of teratoma which afflicts him.

When irradiation and orchidectomy have caused the complete disappearance of clinical and biological evidence of a uniform round cell radiosensitive embryonal carcinoma, the prognosis is good. Should metastases appear later, an apparent complete cure may still be attained with early treatment. These patients should, accordingly, send their urine in for hormone bio-assay every three months during the first year and every six months for the next two years or more.

Complete regression is seldom attained with the true mixed cell or teratoid type of teratoma. Irradiation can cause all clinical signs to disappear, but the hormone may only decrease in amount to a minimum which remains present in spite of irradiation. In other cases there is a complete loss of hormone elaboration at the end of the treatment, but in a relatively short time the hormone output will rise precipitously. These patients with a mixed cell type of teratoma should have their urine examined every month for the first six months after the initial irradiation. The frequency of bio-assay after that may be determined by the evidences of the presence of the disease.

Important as this procedure is to the patients' health and to the length of survival, it is difficult to make the patients remember the little matter of having their urine examined. Many clinics aid the patient by notifying him at the time that a bio-assay should be performed. Owen and Cutler[24] find it efficacious to send the patient a 100 cc. bottle containing a drop of tricresol before every scheduled time for a bio-assay. Instructions for collecting a sample of the first morning urine should be enclosed.

When the hormone test becomes positive in one of the follow-up tests after having disappeared following irradiation, the patient should be advised to return for examination and very probably more radiation. Those patients in whom the hormone did not decrease below 100 to 300 mouse units per liter may show very little change for some months. If the hormone increases appreciably, they should be given more irradiation. There are records of some of these cases who have been irradiated several times in a period of six months, in whom the hormone disappeared for variable lengths of time. The length of survival was apparently increased. The treatment of choice and the progress of these patients is always uncertain.

The possible bad effects that may arise from irradiation must be borne in mind by the clinician. These effects may not be evident until some time after irradiation is started. Careful observation of the patient is necessary so that doses of irradiation may be changed when impending injury becomes apparent. The technique devised by Ferguson[12] which incorporates Coutard's divided dose method, is claimed to greatly reduce the incidence and degree of radiation sickness. By Ferguson's technique, the severe nausea and vomiting with dehydration and loss of 20 to 30 pounds of weight after radiation of the abdomen has been largely eliminated. Many of Ferguson's patients gained weight; a loss of 5 pounds was exceptional.

Other more serious complications arise in people whose internal structures appear to be sensitive to the Roentgen rays. Fortunately, these are rare cases but the course in such individuals is usually fatal unless their abnormal reaction is recognized early enough to change the radiation treatments. The reaction is apparently an initial erythema followed by a heavy fibrosis. Acute ulcers in the stomach and ileum have caused death following irradiation of teratoma metastases and carcinoma of the uterus. Benign strictures of the small intestine have also been noted in the latter cases. Brunschwig and Fox[3] had a patient who died six months after receiving an apparently beneficial irradiation of 2,362r. to the abdomen for teratoma testis. The only complaint had been pain and severe cramps in the upper abdomen. Autopsy revealed a diffuse fibrous peritonitis, torsion of the terminal part of the ileum, and gangrene and multiple adhesions of the first part of the transverse colon. Owen[22] administered "fourteen doses" of irradiation to chest metastases of teratoma testis two and one-half years after the last abdominal irradiation. There was regression of the tumor mass, but later signs of pulmonary involvement became pronounced. Autopsy two and one-half months later disclosed massive pulmonary congestion and some fibrosis with no signs of malignancy in the lungs. There had been no evidence of heart disease. The outcome of these complications is not usually manifest until some time after the irradiation. Signs of abdominal distress or pulmonary weakness that come on during the course of the exposures may indicate sensitivity, and the decreasing or discontinuing of the dosage may prevent severe consequences. They can not otherwise be foreseen or prevented.

In the three year period of the use of Ferguson's method at the time he wrote his article he had obtained 48 per cent one to three year cures compared with 37 per cent one to three year cures with the old method. Using 200 kilovolts and 30 milliamperes the (1) distance was increased from 50 cm. of the old method to 70 cm., with some metastases being radiated at 100 cm. distance; (2) filtration was in-

creased from 0.5 mm. copper to 1.5 or 2 mm. copper or aluminium; (3) daily doses to each portal decreased from 850 Roentgens to 400 Roentgens and later, for the radioresistant tumors, to 100 Roentgens; (4) total dose divided over a long period of time increased from 850 to 4,000 Roentgens. The usual portals are used with the two daily exposures being applied to different regions so as to avoid nausea and possible deep tissue damage from cross-firing. This small dose method protects the skin and gives a greater accumulative lethal effect at a depth of 10 cm.

Ferguson found that the increase in three year survivals was largely due to the favorable response of many of the radioresistant tumors to small frequent doses of 100 Roentgens at a distance of 100 cm. with filtration of 1.5 or 2 mm. These doses may be given daily over long periods of time to a total dose of 4000 Roentgens. The radiosensitive teratoma require more intensive irradiation.

Recently, a few newer Roentgen ray machines developing 600 to 850 kv. have been tried with very good results. At the California Institute of Technology where 850 kv. are used, the entire trunk is exposed to irradiation if metastases are indicated by the hormone test, even though they are not clinically evident.

RADICAL SURGERY

The complete extirpation of the primary tumor and its primary and intermediate secondary lymph zones is at present the only known method of curing adult teratoma and the highly radioresistant tumors in the teratoid, mixed cell, group. No distinction of the type of teratoma present was formerly considered in deciding upon operation as the treatment of choice. The absence of clinical metastases was the main criterion. As the use of irradiation became the choice of treatment by practically all clinicians, the use of Chevassu-Hinman operation has become more infrequent. The value of its use is still maintained by able surgeons who have had considerable experience with this disease.

The operation requires a surgeon who has thorough knowledge of the local anatomy. The stripping of the peritoneum adjacent to the bladder and the lower part of the iliac vessels, and the attempt to remove all the glands on the left side make the procedure difficult. Although the early results were disappointing, those of the past ten years show that it has a definitely positive value in the properly chosen cases. In 1914, Hinman[16] reported an 11 per cent operative mortality in the cases handled by various surgeons. Cairns[4] performed radical surgery on nineteen patients in England with no surgical deaths. Five of the nineteen lived without signs of recurrence, although one died later from another cause. In 1933, Hinman[17] showed a 17 per cent five-year cure in 109 cases. There was one operative death from pneumonia in ten days. Twenty of the cases were found to have inoperable metastases after retroperitoneal resection was done. Forty-one of the other eighty-nine cases had preaortic metastases. Eighteen of them survived two or more years. Four were known to be among the five-year cures. The prognosis of most of the patients in the group living between two to five years was considered good. The results of Hinman's[15] own fourteen cases of radical surgery, published in 1935, disclose ten patients living from one to ten years. All had a *good* prognosis. Seven of the fourteen patients had had metastases, yet four of them had survived one to fourteen years with good prognosis for further survival. It is significant that eleven of the fourteen cases were the radioresistant mixed cell teratomata which otherwise would have been without hope. One was chorionepithelioma and died one and one-half years later with metastases.

The operation has undoubtedly saved the lives of a number of individuals who had the radioresistant teratomata. Some of these patients had abdominal metastases, and irradiation might only have prolonged their life a few years at the best.

The choice of radical surgery must be governed by the following factors:

1. The patient must be in good physical condition.

2. There must be no clinical evidence of metastases. It is better to ascertain that the duration has been less than four months, since metastases are common at six months.

3. Therapeutic irradiation must have had but little or no effect on hormone excretion. Intensive irradiation of the testicle in five days followed by orchidectomy should be combined with the hormone test.

4. Histologic structure, preferably after irradiation, must indicate radioresistance.

There are several limitations to the treatment which give it some uncertainty, but they are not significant enough to prohibit its choice.

1. All the lymph glands have not always been removed. The superior mesenteric artery makes it difficult to reach all the glands on the left side. There may be some invasive metastases between the vena cava and the aorta whose complete removal may be doubtful or impossible.

2. There may have been a spread through the blood stream. This is not uncommon in the teratoid type of testicular tumor.

3. Lymphatic metastases may have progressed beyond the scope of surgery. This places emphasis on the restriction of operating only on known early cases.

Ferguson[11] asserted that these contingencies plus the fact that irradiation has cured patients with metastases above the limit of the surgical field shows that the operation "disregards the normal pathogenesis, and is based on false premises, and should be entirely discarded."

If the operation is limited to the radioresistant tumor, some patients with beginning abdominal metastases may be saved. Even irradiation will not save those with chest metastases that are beyond the reach of the surgeon. The failure to remove all the lymph glands must be feared, but the magnitude of its importance is discounted by the percentage of cures achieved. If it is felt that metastases are present, or their presence is seen in a frozen section of a removed gland, another small incision low on the left abdomen will make removal of the lower lymphatics along the left iliac vessels more certain. This is presuming that the main incision is on the right side, as recommended by Hinman, regardless of which testicle is teratomatous. The presence of venous metastases is a fear in every case. Restriction of the operation to early cases is essential. The use of roentgenograms of the lungs may reveal pulmonary metastases and prevent a useless attempt at surgery when they are present.

The potentialities of the radical operation are expressed in the relatively high percentage of five-year cures of the radioresistant teratoma, and in the fact that the prognosis is good in nearly all patients after a two-year survival. The available records indicate that the five-year cure will be higher than 17 per cent. The operation is not hazardous, but it must be complete. It requires an experienced surgeon with the perseverance necessary to search for thoroughly and remove all the glands.

The choice of this procedure must be limited to those cases in which the onset of the tumor is recent; the radioresistance of the teratoma must have been demonstrated by the poor effects of irradiation on hormone production and by the unaltered histological picture after irradiation. In this group it offers a hope of cure to men in whom no other means of help is available.

In summary, it may be said that the result of the most recent innovations in pathological research (Maner) indicates that in testicular tumors no new growths of a single cell type exist: that, if sufficient pains are exerted in the search, cells typical of all germ layers will be found represented as taking part in the wild growth. This finding greatly increases our realization of the potential danger of testicular tumors.

The efforts of the roentgenologists (Cutler, Dean, Ferguson) have shown that

widespread radiation in fractional small amounts is a necessity as a means of encompassing the entire lymphatic bed over which the wild cells may be advancing. They have pointed out that all tumor types should be put to the therapeutic test of irradiation which should be instituted both before and after orchidectomy. Responses to radiation should be measured both by an accurate determination of the degree of shrinkage of the primary testicular growth by measurement with calipers and by a determination of the disappearance or reduction in the amount of hormone in the urine through repeated bio-assays before, during, and after treatment.

To the endocrinologic researches of Zondek, Evans, and Powell, we owe the recent knowledge that the hormone produced by the testicular tumor and poured out in the urine closely resembles the pregnancy hormone in its bio-assay. Its presence gives a direct indication of radiosensitivity and in general its fluctuation under treatment provides us with an index of the effectiveness of the efforts being exerted to cure the disease.

Finally, to the surgeon and anatomist (Hinman-Chevassu), we owe a knowledge of surgical approach and surgical method which permits us to eradicate the original tumor by wide excision including the primary lymphatic nodes in front of the aorta to which the tumor may have extended. This they have shown is the only means of hope for life in those individuals afflicted with a chorionepithelioma or in those in whom a radioresistant tumor with cells of the adult type exists.

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[From Fernelius' Universa Medicina, Geneva, 1679.]

BOOKSHELF BROWSING

MEDICINE IN ENGLAND IN 1837

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THIS particular year happened to be in a period which was one of the most outstanding in the history of medicine in England. When one realizes that such distinguished men as Bright, Addison, Argyll-Robertson, Hodgkin, Stokes, Graves, Corrigan and Herberden were writing at this time one can readily recognise its importance in medicine. It was with the greatest interest that the author reviewed these journals of one hundred years ago. The more one read the more fascinated one became. It also had a very salutory effect. It is considered that we have recently made tremendous advances in medicine, but a review of this period will have a most humbling effect. It will be discovered that many things which one looked upon now as new were known to these older clinicians and even if they could not prove the mechanism, their faculty of reasoning was so sound that they arrived at the correct explanation. The mastery of clinical description far exceeds that seen in the present day medical journals. Many young authors could profitably spend time studying their methods before they started writing articles of their own.

This era was shortly after the introduction of the stethoscope into clinical medicine by Lannec and there was still debate as to its value. Many clinicians felt that there was a tendency to neglect the symptoms and critical observation of the patient and depend wholly on the findings by auscultation. The abler clinicians used both to their full advantage and found that they were supplementary. One can see a strong similarity to the dispute as to laboratory methods in medicine at the present day. During this period confirming the diagnosis in the dead house seemed to be the method of scientific approach to clinical medicine. Accurate bedside observations were made and then at the autopsy table the findings were checked. One cannot help feeling that many of the classical observations of disease which have been published could not have been done had this not been the method of approach. It is a method not sufficiently prevalent at present and it seems likely that there would be many fewer diagnoses of unusual conditions were they to be checked by the findings at autopsy. Most of the brilliant men at this time were physicians, but apparently considerable surgery was done although anesthesia and antisepsis had not been introduced. The results were astonishingly good, although one assumes, as at present,

that relatively few of the bad results found their way into print. Genito-urinary surgery seemed to be fairly extensively practiced at this time and calculi appeared to be very common as there were many articles regarding the removal of stones, mostly by crushing. In obstetrics, cesarean section seemed to be attended with great risk as there were many articles recounting success with this procedure. In treatment blood letting was beginning to wain, although leeches were still popular. Purgation also appeared to be one of the usual procedures but many authors were doubtful of its value unless used in moderation. Syphilis was apparently then as now a problem and was treated by intensive mercurial therapy. The drug was given until signs of mercury poisoning appeared and then a so-to-speak maintenance dose, short of toxicity, was administered.

One is struck by the excellence of the journals which compare very favorably with those of to-day. They might be divided into two classes: review journals and journals for the publication of original articles. Four of the journals are still published; *The Lancet, The Edinburgh Medical and Surgical Journal* (now the *Edinburgh Medical Journal,*) *The Dublin Journal of Medical Science,* and the *Guy's Hospital Reports. The Transactions of the Provincial Medical and Surgical Association* subsequently became the *British Medical Journal. The London Medical Gazette* which was also published has been given up. The review journals were the *British and Foreign Medical Review* and the *Medical and Surgical Review.*

The review journals were excellent. They gave reviews of three types on all phases of medicine. The first part was devoted to analytical and critical reviews. This meant exactly what it said. The reviews gave the data on the subject and praised what the reviewer believed to be true, but harshly criticised what he considered false. They appeared to be much better than those at present which are mere compendiums of information. The second part was devoted to reviews of recent books. In the *British and Foreign Medical Review* there is a review of a book on "Practice of Medicine" by Richard Bright and Thomas Addison. It was written for students. The reviewer thought it was rather a poor book and was particularly scathing in his criticism of their treatment of fevers. He said they were too fond of active mercurials and purging in this condition and that they did not mention leeching or the use of the warm bath which he had found most beneficial, particularly in children. The reviewers do not give their names so one does not know whether they were famous or not. The third section is devoted to brief abstracts of articles appearing in foreign journals.

In the journals devoted to original articles there were none of the classical descriptions of disease but many famous names in medical history contributed. I have selected some of the publications of these men for description as details of all that was published cannot be given.

The Lancet proved to be one of the least interesting of the journals. The popular type of article in this periodical appeared to be the publication of lectures both theoretical and clinical which had been given as a series to students or practitioners. There was a series of lectures by Magendie on the Physiology of the Nervous System, which he had delivered in London. Also several articles by Marshall Hall on Medicine, much of the time being devoted to the nervous system in which he was especially interested. Much space was devoted to lectures by Professor A. T. Thomson on Medical Jurisprudence and Dr. George D. Sigmond on Materia Medica. There was also an article by Warren from the Massachusetts General Hospital on the Diagnosis of Abdominal Tumors.

The London Medical Gazette contained much of interest. There was a large series of clinical lectures by Graves on a wide variety of topics. He described the findings, gave a critical analysis of the symptoms and signs and discussed admirably the differential diagnosis as well as the treat-

ment. This type of article seems to have largely disappeared but one can see where it would be of immense interest and value to the general practitioner to have analyses of this type by a master clinician. In discussing fever he protests against purgation. He thinks venesection useful at the very beginning but not later, and says it should never be done if there is a macular eruption. He describes a case which had been seen by Corrigan who made the correct diagnosis of abdominal aneurysm as confirmed by autopsy. The patient's complaints were gastro-intestinal but there was a very feeble pulsation just below and to the left of the ensiform cartilage. In a letter to Graves which he publishes, Corrigan states that he made the diagnosis on the following points: (1) The presence of a bruit de soufflet over the feeble pulsation which increased on lying down. Corrigan believed this to be due to the removal of the effect of gravity thus rendering the wall of the aneurysm more lax. (2) The localisation of the bruit to the particular area where the feeble pulsation was felt. In another article, Graves discusses the physiology of the motor powers which cause and regulate the circulation in normal states and in inflammation. This article contains many facts which have been confirmed by recent investigations of the peripheral circulation and which one had supposed were relatively new. There is also an article by Graves on Influenza.

A letter from Graves comments on the recent continental enthusiasm concerning the part of reflex nervous action in causing sensations in parts removed from the real seat of action. He states that stimuli acting on nerve terminations at one point can produce pain at some distant point. He claims that he was first to describe this mechanism, which he did in the *American Journal of Medical Sciences* in August, 1836. Marshall Hall later writes a letter in which he states that he described it in a Zoological Journal four years earlier.

Heberden published an article on Nervous Disorders. McGregor the pharmacist to Glasgow Infirmary wrote concerning the state of urea in healthy and diseased urine. He says that he had found urea in the blood in cases of suppression of urine but never in normals although he had used many pounds of serum. He evaporated the urine or blood to dryness, then dissolved the urea out with anhydrous alcohol. He dried it again and the difference in weight he interpreted as urea.

There is a short note on Matriculants in the Medical Schools of America. The numbers are:

University of Pennsylvania—380,
Lexington Transylvania University—277,
Cincinnati Medical College—122,
Louisville Medical Institute—100,
Harvard—82,
Medical College of Ohio—80.

Guy's Hospital Reports contained two articles by Thomas Addison; one on pneumonia in which he stated that there was no pain unless the pleura was involved, and the other on treatment by electricity. He used static electricity, one terminal being placed on the symphysis pubis and the other on the sacrum. There were also two papers by Richard Bright. The first—Cases and Observations illustrative of diagnosis when tumors are situated at the base of the brain, or when other parts of the brain and spinal cord suffer lesions from disease. The second—Observations on Abdominal Tumors and Intumescence illustrated by cases of encephalocyst hydatids. He had fifteen cases of hydatid cyst in the abdomen and considered that the only treatment was drainage. Hodgkin published an article on a remarkable specimen of urinary calculus and discussed the structure and form of urinary calculi.

The Dublin Journal of Medical Science contains two excellent articles by Corrigan. In a discussion of bruit de soufflet he states that he has never seen it unless there is narrowing or permanent patency of an orifice. He says that it can also be heard over arteries when they are dilated and can be produced by pressure on them. He believes that it was due to a current like action of the blood tending to cause vibra-

tions of cavities or arteries when they are relaxed. He states that the thrill was due to the same cause. He illustrates his view by many examples. In a later article Dr. Nagel violently disagreed with Corrigan basing his views principally on the uterine souffle but did not offer a theory of his own. Corrigan's second article was on Aortitis as one of the causes of Angina Pectoris with observations on its nature and treatment. He states that there are two types of aortitis which can cause angina pectoris: (1) inflammation of the lining membrane of the aorta with submucous infiltration and effusion of lymph. He states that the inflammation causes a pulpy character of the aorta above the valves and blocks the coronary vessels. Sometimes a membrane may close their orifices. (2) marked atheroma. One makes the diagnosis by exclusion of other diseases which could cause the symptoms rather than by direct signs produced by the disease itself. His treatment was local bleeding with leeches, counter irritation and the exhibition of mercury until the mouth became sore.

There is an article by Purkinge on the discovery of ciliary motions in the cavities of the brain and a review of a book by William Stokes—Treatise on the diagnosis and treatment of diseases of the chest. In his introduction he states that the good physician should use a close correlation of symptoms and physical signs so as to illustrate the bearing on diagnosis and remove the unjust opprobium on the advocates of auscultation that they neglect the study of symptoms.

The Edinburgh Medical Journal has a paper by Argyll Robertson on Extraction and Displacement of Cataract with tables showing relative success from the performance of this operation.

There is also a review of one volume of Principles of Surgery by James Syme, Professor of Clinical Surgery, Edinburgh University. In discussing cancer of the breast Syme divides the patients into three classes: (1) good risk—disease circumscribed, slowly progressive and not attended with grandular involvement; (2) operation may be performed but unlikely to be successful—glands tainted but within reach; (3) operation improper—where glands cannot be removed. He states that in old age the disease advances slowly and operation should not be performed. Wherein does this differ from present day views?

There is an announcement that this year was the centenary of the Royal Medical Society of Edinburgh. This society is a student society in which papers are presented by students and on occasion by distinguished physicians. The students join freely in the discussions. It has a fine hall and an excellent medical library.

In conclusion the author feels filled with admiration at the careful study which the physicians of a hundred years ago gave to their cases and at the deep thought which was expended both on the particular case and on the general problem of disease. It seems probable that the pace at which one lives to-day has altered things so that the same serious and discriminating contemplation is not indulged in.

BOOK REVIEWS

PEDIATRIC UROLOGY. By Meredith Campbell, M.D., F.A.C.S. With a section on Bright's Disease in Infancy and Childhood. By John D. Lyttle, M.D. With over 1350 illustrations on 610 figures and two colored plates. In two volumes. The Macmillan Company, 1937. Price $15.

This well done work by Meredith Campbell is timely. Also it is needed and, we hope, will enjoy wide distribution. For only recently has pediatric urology engaged the attention of any but a percentage of those who label themselves urologists or pediatricians.

We know that about half of all children, at some time, suffer from some urologic disturbance. In the great majority of instances these complaints are overlooked, or diagnosis and treatment are directed to a distant part of the body. This is because the urologist has neglected the child (except when the urological condition has been only too apparent), and until the last decade the same can be said of the pediatrician.

But at present an ever increasing interest in the clinical problems of urology in the young has taken place. The development of miniature cystoscopes has added or awakened this interest.

The author says: "It is hoped that these pages will help to make medical advisers of the young more urologic-minded and that, in turn, urologists will see their young patients, in part at least, through the eyes of the pediatrist."

The section on Bright's disease in infancy and childhood by John D. Lyttle is excellent and sound teaching. Urologist, pediatrician, internist, and the man in general practice can well linger through this section.

Volume One (576 pages) covers: Methods of Examination and Diagnosis, Obstructive Uropathy, Anatomy, Physiology, Embryology and Anomalies of the Urogenital Tract, Urinary Infections (Non-tuberculous, Tuberculous, Unusual Types), and an Index. Volume Two (540 pages) covers: Bright's Disease, Genital Diseases, Urogenital Injuries, Calculus Disease, Tumors, Neuromuscular Disease, Enuresis, Urosurgery, Author's Bibliography, and an Index.

The illustrations are of a high order. It should be sufficient to hint that inasmuch as Dr. Campbell is the author, the work is authoritative, but one will not read far until he senses a master teacher, scientist and urologist standing behind the printed words.

We have nothing but praise for this work, and can but repeat ourself . . . Dr. Campbell has done a needed and outstanding work.

TEXTBOOK OF DIAGNOSTIC ROENTGENOLOGY. By Lewis J. Friedman, M.D. 638 illustrations. D. Appleton-Century Company, Inc., 1937.

Dr. Friedman has written to the point in covering this broad subject in 623 pages. And, withal, he has not neglected any part of his subject. He has used judgment in what to cover in a couple of short paragraphs and what to give the minutest detail. In rereading the Contents again, one is struck with the thought that in every sense of the word it is a text book and that the subject has been treated from A to Z.

Of course, it was written mainly for the radiologist but surgeons may well study it. Diagnostic Roentgenology plays a large role in surgical diagnosis, and the surgeon would do well to learn to talk the language of the radiologist. The senior year medical student or the interne would put out money he could consider well spent if he possessed this volume, and then made it a part of his daily reading.

For, Dr. Friedman has written a solid book on an important subject, and without trying to be "popular" has made it readable and interesting. We gladly recommend it to all who are interested in this subject.

OPERATIVE SURGERY. THE EAR, AIR PASSAGES AND NECK. By Dr. Martin Kirschner with the collaboration of A. Lautenschlager and Dr. O. Kleinschmidt. Authorized translation by I. S. Ravdin, M.D., and George M. Coates, M.D. With 460 illustrations, mostly colored. J. B. Lippincott Company, 1937.

The illustrations (mostly in color), alone make this work worthwhile. In addition, the

text-matter (528 pages) is solid and authoritative. Doctors Ravdin and Coates have done an excellent translation.

The book contains, in the main, the surgery of the head and neck exclusive of the brain and certain aspects of the surgery of the face.

We are told that "There is at present no single work which covers the exact field covered by this one."

The general surgeon and the specialist will find this work a great help to him. It is a book that is not published every day, and one that a physician is more than fully satisfied with after purchasing. From every angle . . . well done.

THE FUNDAMENTALS OF ELECTROCARDIOGRAPHIC INTERPRETATION. By J. Bailey Carter, M.D. Charles C. Thomas, 1937.

This is a work every internist and, in fact, every general practitioner should read with care and thoroughly assimilate as he goes along.

It is of interest to the surgeon only in the fact that some of this class desires to have a slight acquaintance or understanding of any thing in medicine that aids in making a diagnosis.

Doctor Carter has written an excellent and needed book. It is just the book to give an interne beginning his medical service. It is well illustrated (250 of them), contains an exhaustive bibliography, a glossary, and index. A book that should enjoy a large and wide distribution.

SOURCE BOOK OF ORTHOPAEDICS. By Edgar M. Bick, M.A., M.D. The Williams & Wilkins Company, 1937. Price $4.00.

This book of 376 pages, with a bibliography and an index, is a comprehensive history of the beginning and rise of orthopaedic surgery. One gets a clear conception of the struggles of the pioneers during the days when this branch of medicine was merged with medicine and surgery and not a clearly defined specialty.

The author devotes chapters to such interesting subjects as Primitive Man and Ancient Practice, Middle Ages, Renaissance, 17th Century, and then the last half of the book is devoted to the Modern Period and considers under it Physiology, Bone Surgery, Joint Surgery, Muscle Tendon Surgery, Non-operative Orthopaedics, and Rise of Orthopaedic Hospitals and Institutions. In an Appendix is given Orthopaedic Periodicals.

Dr. Bick has written a valuable book. Anyone interested in the various phases of medical history will find it good reading; the man who does orthopaedic surgery will find it a book that will prove a stimulus and aid to him in his work.

CARCINOMA OF THE FEMALE GENITAL ORGANS. By M. C. Malinowsky and E. Quater. Translated from the Russian by A. S. Schwartzman, M.D. Bruce Humphries, Inc., Boston, 1936. Price $5.00.

The original work was written by eleven authors, eight "Professors," one "Privat-Dozent," and two "Doctors," and has been well translated by Doctor Schwartzman. It is a compact book of 255 pages, 50 figures and two colored plates, and we quote from the Foreword, "Being motivated by the desire to present the problem of carcinoma of the female sexual sphere from various viewpoints, an attempt was made to discuss it on the basis of the newest data available at this time. In order to deal with the individual questions not only on the basis of literature-data (even the newest) but also on the basis of large personal experience, specialists in various branches of medicine have been invited to contribute to this work. We believe that such method of approach enables us to present to the reader, if not an exhaustive, at least a sufficiently thorough elucidation of the problem of carcinoma of the female sexual sphere."

There is no index but it is that type of book one reads as one does a novel. Those concerned with this problem, especially gynecologists, will find it time well spent to linger through the pages of this work. They will discover fresh viewpoints, and much that will stimulate thought.

THE TECHNIC OF LOCAL ANESTHESIA. By Arthur E. Hertzler, A.M., M.D., PH.D., LI.D., F.A.C.S. Sixth Edition. The C. V. Mosby Company, 1937. Price $5.00.

When a book appears in a sixth edition there is little or no need of saying more than to hint it must be a good book, that it must give the reader that which he seeks and wishes

to know, and to anyone who wishes information on the technic of local anaesthesia here is the work he should turn to.

This edition has been revised in part, simplified here and there, and some material has been added. The chapter on spinal anaesthesia has been carefully revised by Dr. Irene A. Koeneke. The book is 284 pages long, has 142 illustrations, and an Index. These days it is necessary to do many operative procedures under local anaesthesia, many surgeons leave this detail to an assistant or an interne, and, in the end, resort to a "whiff of gas" to complete the operation. These men, especially, would do well to own and then carefully read this interesting and instructive work.